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ENDEAVOUR

The British quarterly scientific journal ENDEAVOUR was first published, by Imperial Chemical Industries Limited, in January 1942. Its purpose is to provide scientists, especially those overseas, with news of the progress of the sciences. While emphasis is laid upon British work, narrow insularity is avoided by publishing numerous articles from overseas contributors and by impartial reference to the world's scientific literature. To make the journal truly international in character it is published in five separate editions—English, French, German, Italian, and Spanish.

No charge is made for ENDEAVOUR. It is distributed to senior scientists, scientific institutions, and libraries throughout the world, the guiding principle being that of helping scientists overseas to maintain those contacts which their British colleagues have always so much valued. Within these limits the Editors are at all times glad to consider the addition of new names to the mailing list.

The drawing on the cover is of the bark Endeavour, *which, commanded by Captain James Cook and carrying a number of scientific workers, was sent out by the British Admiralty in* 1768 *to chart the South Pacific Ocean and observe the transit of Venus*

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

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Royal patronage of science

It is with pride and pleasure that we publish overleaf a personal message of goodwill to ENDEAVOUR from H.R.H. The Duke of Edinburgh. His Royal Highness has already honoured us on two previous occasions, by presenting the ENDEAVOUR prizes at meetings of the British Association for the Advancement of Science, and we are deeply grateful for this further token of his interest in the progress of the journal. It is fitting at this moment, when the British Monarchy enters upon a new phase, that we should express our loyal devotion to Her Majesty Queen Elizabeth II and to her Royal Consort.

Royal patronage of science has always been a feature of civilization, though in early times it was sporadic and fickle, and was usually inspired by the (not at all unworthy) hope of enlarging the royal or national income. Thus the first of the Plantagenets, Henry II, who received much revenue from the madder industry, encouraged the madder-growers by ruling that red coats were to be worn in the hunting field—an action paralleled by a much later French king, who dressed his troops in red trousers. It is foolish to decry such acts as mercenary, for one of the principal aims of science is to enrich the material side of life, but our heritage from Greece makes us feel that a nobler aim is to promote science for the mere sake of widening the bounds of knowledge. Such a motive is to be found here and there among princely figures throughout history. The great 'Abbāsid caliph Al-Ma'mūn, for instance, who ruled from 813 to 833 A.D., encouraged scholars of all persuasions, including scientists, and founded at Baghdad a scientific academy which was equipped with a library and an observatory.

A similarly enlightened ruler was the thirteenth-century '*stupor mundi et immutator mirabilis*,' the Emperor Frederick II, himself a philosopher and man of science. His court in Sicily was thronged with learned men, most of them Jews and Muslims but some, such as Michael Scot and Fibonacci, Christians. He delighted in exploding superstitions by direct experiment, and spent a great part of his leisure in writing a treatise on falconry, in which many facts about the anatomy of birds are recorded for the first time.

In Britain, Royal interest in scientific matters is first well exemplified by James IV of Scotland (1473–1513), whose marriage with Margaret Tudor paved the way for the union of Scotland and England a century later. He was not content with speculation and theorizing, but carried out experiments in chemistry, physiology, and medicine. Though his niece, Elizabeth I (1558–1603), was not a practising amateur scientist, she too was interested in the subject, and William Gilbert (her personal physician and the author of the celebrated treatise on the magnet), was frequently commanded to perform experiments before her. Elizabeth also lent her support to exploratory navigation.

We may pass by the first of the Stuarts, James I (1603–25), whom Henri IV of France is said to have described as 'the wisest fool in Christendom,' and go on to Charles I (1625–49), in whose reign William Harvey published his discovery of the circulation of the blood. The King took an intelligent interest in Harvey's work, as in his further researches on embryology, and often asked for demonstrations to be made before him and his court. The 'Merry Monarch,' Charles II (1660–85), as acute a mind as ever ruled a kingdom, seems to have been amused by the gullibility of some of the contemporary scientists, but proved his genuine belief in the potential value of science by granting its first charter to the Royal Society.

In more recent times, the services to science of George III (1760–1820) are well known. He encouraged Captain Cook's voyage (1768) which is commemorated in every issue of ENDEAVOUR, and entrusted direction of the royal botanic garden at Kew to the celebrated Sir Joseph Banks. He also formed a comprehensive collection of scientific instruments, intended mainly for the instruction of the Royal children, and took a personal interest in his private observatory at Kew.

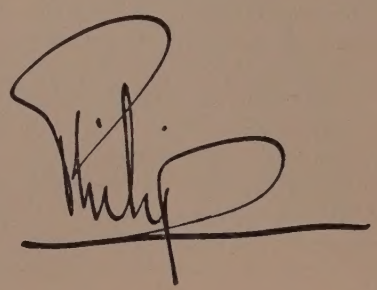
Still more recently, Prince Albert's services to science and technology played an invaluable part in the scientific revolution of the nineteenth century. It was to his influence that the Exhibition of 1851 was mainly due; he did much towards establishing the scientific side of agriculture; and in 1845 he became first president of the Royal College of Science (now part of the Imperial College of Science and Technology).

The tradition of Royal patronage of science is thus well established in Britain, and not only British scientists but those of all nations will take pleasure in the fact that the tradition is being so admirably maintained by Her Majesty The Queen and His Royal Highness The Duke of Edinburgh.

BUCKINGHAM PALACE.

"Endeavour" is doing a wonderful job keeping general readers, as opposed to specialists, informed of the progress of scientific research and technology in this country.

I hope that the journal will never be short of readers; I am sure it will never be short of material.



A chemical phase in the transmission of nervous effects

SIR HENRY DALE

Satisfactory experimental evidence exists that impulses are transmitted within single cells, such as a muscle or nerve fibre, by an electrical mechanism, and it has thence been argued that impulses are similarly conveyed from one cell to another. There are, however, serious objections to theories of electrical conduction across such cell-junctions. For some fifty years, evidence has been accumulating which indicates that transmission at these points occurs by chemical means, and that a principal agent involved is the ester acetylcholine.

It is now generally accepted that a wave of excitation, or impulse, is conducted within the limits of a living, excitable cell, such as a muscle or nerve fibre, by a process producing an electrical stimulation of successive points on its surface. In recent years the application of electronic methods of amplification and recording to the large fibres found in some cephalopod nerves, and the use of exceedingly fine capillary electrodes for insertion into them, has enabled rapid progress to be made towards a fundamental understanding of this process. It had long been known that there is a surface potential of the order of 100 millivolts on such a living fibre, the outside being steadily electropositive to the inside when it is at rest; and it is now known that when a wave of excitation sweeps over any point on the fibre this potential difference is not merely diminished by its passage, as was long supposed, but is actually reversed. At the peak of the passing wave, the surface becomes momentarily electronegative to the interior, as well as to the unexcited surface of the rest of the fibre. It is known, further, that this reversal of polarity is due to a specific change in the surface membrane, of such a kind that sodium ions pass through it into the fibre from the external medium and potassium ions outwards from the interior, and that this process is reversed as the excitation subsides and the positive surface potential is restored. Meanwhile, however, the negativity at the excited spot has caused local electric currents to flow into it from neighbouring points at rest, and the local cathodes so formed cause new points of excitation. Thus with successive new points of excitation and negative potential, the impulse is conducted rapidly, in both directions, by a mechanism which is essentially electrical, though the excitatory change in the surface membrane must have a chemical basis, as yet unknown. A similar process is effective in a muscle fibre, and presumably, indeed, in an excitable cell of any kind, so long as we are dealing with conduction within the limits of a single cell.

Our direct concern in this article, however, is not with conduction within fibre limits, but with the mechanism by which, when an impulse reaches the end of a nerve fibre where it is in close contact, but not in protoplasmic continuity, with some part of the surface of another excitable cell, the excitatory process is transmitted across the junction. Such nerve-fibre endings are shown in the diagram of figure 1 at *syn.n.e.*, *m.n.e.*, and *postg.n.e.* The receptive cell may be a muscle fibre, either a quickly contracting, cross-striated fibre (*v.m.f.*) of a voluntary muscle, moving the trunk or the limbs, or an involuntary muscle fibre-cell (*i.m.f.*) of a viscus, such as the heart or the digestive canal, or the secreting cell (*gl.c.*) of a gland; or it may be a secondary nerve cell (*g.n.c.*) in a ganglion of the autonomic or involuntary nervous system, itself giving rise to a post-ganglionic nerve-fibre (*postg.n.f.*) ending in its turn in contact with an involuntary muscle or gland cell. In all such cases we have to consider how the effect of a nerve impulse, when it reaches a fibre-ending, is transmitted across the minute breach of continuity in order to produce its effect on the receptive cell.

When an impulse in a motor (*m.n.f.*) or preganglionic nerve fibre (*preg.n.f.*) reaches the synaptic ending (*syn.n.e.*) of that fibre, where it makes contact with the motor end-plate (*m.e.p.*) of a voluntary muscle fibre or with a nerve cell (*g.n.c.*) in a ganglion, it seems to reappear, with only a very small delay at the junction, on the other side of the synapse as a similarly conducted wave of excitation along the muscle fibre, or impulse along the postganglionic nerve fibre. The

transmission is thus unitary, impulse for impulse, and if attention were restricted to cases of this kind it might seem natural to picture the excitatory process as transmitted across the junction by an electrical mechanism, of the same kind as that which conducts the impulses on either side of it. Such an electrical conception of the synaptic transmission is, indeed, still found acceptable, at least as a working hypothesis, by many distinguished neurophysiologists, who apply it to transmission not only at these peripheral synapses, but at all those which figure and function in the central grey matter. Reluctance to relinquish a conception which has seemed obvious is only natural, but there are characters of the transmission of excitation, at all such synapses, which suggest that something occurs there of a kind different from the conduction of impulses within fibre limits.

We shall see that this difference becomes very conspicuous where the effects of autonomic nerve impulses are transmitted to involuntary muscle and gland cells. We ought first, however, to consider certain more general characters, even of the rapid unitary transmission at voluntary neuromuscular and ganglionic synapses, which can be reconciled with the theory of a continuous electrical mechanism only by elaborating subsidiary hypotheses.

(1). The delay in transmission may be brief—it is only about 2 milliseconds at a synapse in a ganglion—but nevertheless is too long to be accounted for on any simple electrical scheme.

(2). We have seen that the impulse in a nerve or muscle fibre is conducted equally in both directions from a stimulated point. Transmission across a synaptic contact-junction, on the other hand, is strictly unidirectional; the excitation passes only from nerve-ending to responsive cell, and never in the other direction. Subsidiary hypotheses have been elaborated, with great ingenuity, to reconcile this one-way traffic across a synapse with an electrical mechanism, like that which conducts the impulse equally either way, but none of them seems to have been convincing. Such a one-way traffic, if carried by local electrical currents, would be expected to go more readily from the bulky muscle fibres and nerve cells to the slender nerve-endings in contact with them; in fact, it goes only the other way. Some additional or different mechanism is clearly needed at the synapses, where this transmission in one direction is fundamental to the co-ordinated activity of the body as a whole. Without it, all bodily functions would break down into chaos. It is to be noted that, as early as 1925, the late Sir Charles Sherrington emphasized the unidirectional nature of the transmission of excitation at synapses in the central nervous system. He also indicated that the cumulative effect of successive impulses, arriving at such a synapse at sufficiently short intervals, necessitated the assumption of the persistence, at that point, of a 'state or agent.' He clearly foresaw the possibility of a chemical phase in the transmission at these junctions.

(3). More than a century ago, Claude Bernard produced evidence of a special chemical sensitiveness at the junctions of nerves and voluntary muscles. He showed that when fatigue, or poisoning with curare, prevented a muscle from responding further to stimulation of its nerve, it was at these junctions that the failure occurred; nerve and muscle on either side of them still responded and conducted normally. Later work by Langley and others showed that the action of curare (or the alkaloid curarine) rendered both the ganglion cells and the voluntary muscle end-plates insensitive, not only to preganglionic and motor-nerve impulses, but to the specific stimulating action of

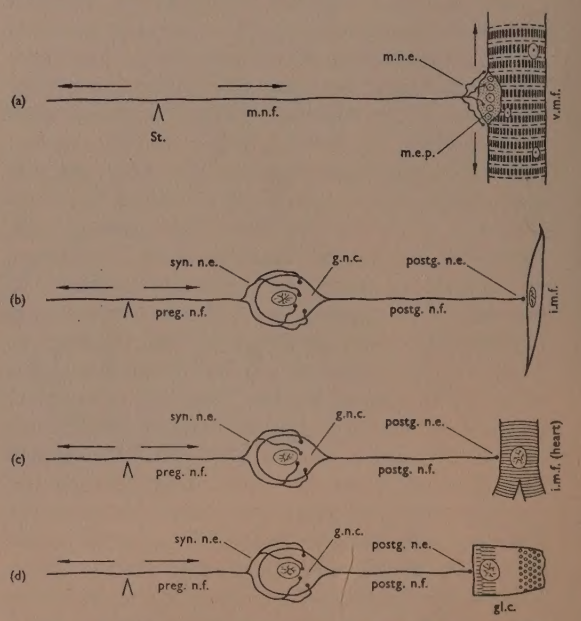


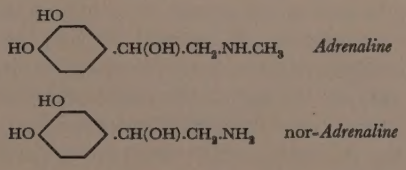
FIGURE 1 – *Diagrams of* (a) *motor nerve fibre* (*m.n.f.*) *with impulse conducted in both directions from point of artificial stimulation* (*St.*). *Its motor nerve ending* (*m.n.e.*) *makes contact* (*synapse*) *with the motor end-plate* (*m.e.p.*) *of a voluntary muscle fibre* (*v.m.f.*). (b), (c), *and* (d) *show preganglionic nerve fibres* (*preg.n.f.*) *of the autonomic system making synaptic contacts with ganglion nerve cells* (*g.n.c.*) *from which arise postganglionic nerve fibres* (*postg.n.f.*), *the endings of which* (*postg.n.e.*) *make contact with involuntary muscle fibres* (*i.m.f.*) *and a gland cell* (*gl.c.*).

nicotine. It is to be noted, as of special significance for our present purpose, that curarine similarly annuls the specific response of these structures to acetylcholine, which, in this aspect of its activity, resembles nicotine. We already get a hint of a chemical, pharmacodynamic phase in the transmission of excitation at these peripheral synapses.

(4). When study was directed to the effects of impulses in autonomic nerves on the layers of involuntary muscle fibres in which they end, the inadequacy of any simple concept of electrical transmission was even clearer. For these impulses do not, like those in voluntary motor nerves, evoke activity in otherwise resting muscle fibres; they modify in one direction or the other—augment or depress—the continuous, automatic activity of tone and rhythm which is characteristic of the involuntary muscle coats of visceral organs, such as the heart, the arteries, or the alimentary canal. Many such organs receive a double nerve supply, from the anatomically distinct divisions of the autonomic nervous system known as sympathetic and parasympathetic; the effects of the two are commonly in opposite directions. Impulses which reach the heart in fibres of the (parasympathetic) vagus nerve inhibit its normal rhythm, or even stop it, while impulses reaching it in nerve fibres of sympathetic origin augment and accelerate the rhythm. Vagus nerve impulses, on the contrary, augment the muscular activities of the stomach and bowels, while sympathetic nerve impulses depress them. There is no ground at all for a suggestion that these impulses, as they pass down nerves of the two divisions of the autonomic system, differ in any way from one another, or indeed, from impulses conducted in other nerve fibres of any kind, anywhere in the body; yet they somehow excite these opposite reactions in the involuntary muscle coats of the same, or of different, organs when they reach the fibre endings, where these make contact with the involuntary muscle fibres. No theory of continuous, electrical conduction across these junctions would account for the contrasted effects.

On the other hand, there were several alkaloids and other natural bases which had been observed to produce effects resembling in a highly suggestive manner those of one or the other of the divisions of the autonomic nerves. Muscarine, for example, a toadstool alkaloid known since 1869, closely imitated the effects of parasympathetic nerves—inhibiting the heart-beat, augmenting the activity of the stomach and bowels, causing a profuse secretion of saliva, etc.; while atropine, from belladonna, abolished these effects of muscarine and most of the corresponding effects of the nerves. On the other hand, adrenaline, from the medulla of the suprarenal gland, reproduced the effects of sympathetic nerves with a comparable fidelity. And, in this case again, an alkaloid (ergotoxine, from ergot) was found which eliminated or depressed the augmentor responses to adrenaline, and the corresponding augmentor effects of sympathetic nerve impulses, and left the inhibitor effects in both cases relatively unchanged. Even where these direct correspondences failed, others as suggestive were revealed. For example, the effect of sympathetic nerves in causing the sweat glands to secrete was not reproduced by adrenaline, but was so by muscarine; and, in this exceptional case, atropine also annulled the effect of the sympathetic nerves, as well as that of muscarine, while ergotoxine did not affect either. Some of these resemblances had been known for many years, long before anybody recognized their true significance, in relation to the mechanism of excitatory transmission from nerve endings to effector cells. It had been customary to account for them by supposing that adrenaline and muscarine produced their effects by respectively stimulating the endings of sympathetic and of parasympathetic nerve fibres.

T. R. Elliott was the first to recognize the true meaning of these similarities. In 1904 he put forward what, at the time, appeared to be the revolutionary suggestion that sympathetic nerve impulses, on reaching the nerve endings, there liberate small charges of adrenaline to produce their corresponding effects, of augmentation or inhibition, on the activities of the contiguous involuntary muscle and gland cells. For many years this hypothesis attracted only a meagre and intermittent attention. One reason for hesitation was to be found, perhaps, in the fact that the correspondence between the effects of sympathetic nerves and those of adrenaline, though striking enough, was not complete. With regard to the divergences, however, it may be convenient at this point to anticipate more recent discoveries which have adequately accounted for them. It has been known since 1910 that actions of the lower homologue of adrenaline, *nor*-adrenaline,



reproduce the effects of sympathetic nerves with a generally closer fidelity than do those of adrenaline itself, but not until forty years later, i.e. in the past few years, was it established that *nor*-adrenaline also occurs, and sometimes predominates, in the secretion of the suprarenal medulla, and, more significantly, that it is often the main component of the chemical transmitter of excitation from sympathetic nerve endings. Certain more striking exceptions to the general correspondence are also accounted for now that it has become clear that the chemical transmitter function does not correspond completely with the anatomical divisions of autonomic nerves; there are some fibres arising in ganglia of the true sympathetic system, such as those already mentioned which innervate the sweat glands, the impulses in which transmit their effects by the release, not of either of the adrenalines, but of the substance which, as we shall see, is in general the parasympathetic transmitter, namely acetylcholine. Thus the anomalous sensitiveness of the sweat secretion to atropine paralysis falls also into line.

Assuming Elliott's hypothesis to be correct, it was obviously necessary to postulate the existence of an analogous transmitter of the effects of parasympathetic nerve impulses. An attempt was soon made, indeed, to cast muscarine for the part; but muscarine was not at all a likely constituent of the animal body, and its stability made its action much too persistent. An agent thus transmitting the effect of a nerve impulse ought to be unstable in the body, so that its action would be not only intense but rapidly evanescent, like that of the readily oxidizable adrenaline. Nearly another decade passed before a suitable candidate came forward for this function, in relation to parasympathetic nerve impulses. Some years earlier, Hunt and Taveau had observed that acetylation of the widely distributed natural base, choline, intensified its depressor activity as much as ten-thousandfold. Having encountered acetylcholine unexpectedly in a natural product, I had the curiosity to examine its activity in greater detail; it was then at once evident that it reproduced the effects of parasympathetic nerves with an even greater precision than that with which the effects of sympathetic nerves were reproduced by adrenaline, and that its action was even more intense and more rapidly evanescent. I guessed, rightly as later evidence showed, that there must be an esterase in the body, to the hydrolytic action of which this choline ester was extremely susceptible. More surprising, however, and even at first sight a little disconcerting, was the discovery that, when these peripheral, muscarine-like actions of acetylcholine were annulled, as they very easily were by a small dose of atropine, another aspect of its activity came into view; it stimulated nerve-ganglia and voluntary muscle fibres in a manner recalling the effects of nicotine. For the sake of brevity, we must here again anticipate later developments, some of which did not begin till 20 years later, in order to make it clear that these other effects of acetylcholine can now be more exactly located, as due to a specific stimulating, depolarizing action on the nerve cells of autonomic ganglia and on the motor end-plates of voluntary muscle fibres.

In 1914, however, a chemical transmission, even of the peripheral effects of autonomic nerve impulses, by the liberation at the nerve endings of substances such as these, was still but a speculative possibility. Even as a speculation it had, in fact, almost ceased to be openly discussed, until Otto Loewi's experiments on isolated frogs' hearts, published from 1921 onwards, gave simple, direct, and convincing evidence of its occurrence, so that the speculation became an experimentally demonstrated fact. The transmitters, liberated into the saline fluid filling such a heart when its vagus and its sympathetic nerves were stimulated, and transferable in that fluid to produce their inhibitor and accelerator effects on another heart, had the characters of acetylcholine in the one case and of adrenaline in the other. Atropine did not prevent the liberation of the vagus-transmitter, but annulled its inhibitor effect on the heart muscle; similarly, ergotoxine did not prevent the liberation of the sympathetic transmitter, but prevented it from accelerating the heart rhythm. There is no longer any reason to doubt that these transmitters are, indeed, acetylcholine and adrenaline. Loewi, with his co-workers, found also that the heart muscle contained the expected esterase, which causes a rapid hydrolysis of acetylcholine into the practically inactive choline and acetic acid, and thus accounts for the remarkable evanescence of its action.

$$\underset{\text{Acetylcholine chloride}}{(CH_3)_3\overset{+}{N}.CH_2.CH_2.O.OC.CH_3\ Cl^-} \rightarrow \underset{\text{Choline chloride}}{(CH_3)_3\overset{+}{N}.CH_2.CH_2.OH\ Cl^-} + \underset{\text{Acetic acid}}{CH_3.COOH}$$

Of special interest and importance for later developments was the further discovery, also due

to Loewi and his collaborators, of the mode of action of the alkaloid physostigmine (eserine). Loewi and others had shown some years earlier that this substance produced its actions by intensifying and prolonging the effects of impulses in parasympathetic nerves; now it was demonstrated that physostigmine depressed, or even arrested, the action of the cholinesterase, and thus protected the liberated acetylcholine and intensified and prolonged its effects. This became of very great experimental importance, in enabling the acetylcholine liberated at nerve endings to be collected and physiologically identified, even from organs which could be kept active only by warm perfusion or by natural blood circulation. It was, indeed, by the use of this protective action of physostigmine and its analogues, and of delicate alternative methods for the recognition and estimation of both acetylcholine and the adrenalines in very high dilutions, that Loewi's original discovery, made on the frog's heart, was progressively extended to the whole range of the peripheral effects of autonomic nerves on involuntary muscle and secreting glands, in mammals as well as in amphibia. It thus came to be generally accepted that all the effects of autonomic nerves are transmitted by the liberation at their fibre-endings of one of these two chemical transmitters—acetylcholine or the adrenalines. And since, as we have seen, these alternatives do not correspond completely with the anatomical origins of the nerves concerned, we may conveniently use a functional terminology which I proposed in 1934, and say that post-ganglionic fibres of parasympathetic nerves are predominantly 'cholinergic,' and those of sympathetic nerves predominantly 'adrenergic,' but that the converse relation is found in a minority of cases.

So far as adrenergic transmission is concerned, this appears to be the end of the story, for no other adrenergic nerve fibres than these postganglionic, autonomic, mostly sympathetic ones, have yet been identified with certainty anywhere in the whole nervous system. There is another respect in which the effects of adrenergic nerves appear to be peculiar: they alone have been found to receive a direct reinforcement from the fluctuating secretion of their transmitter, adrenaline, into the general circulation from an endocrine organ, the suprarenal medulla. At the call of emergency, or of emotional stress, a sudden gush of adrenaline from this organ causes a general and simultaneous evocation throughout the body of the involuntary muscular and glandular reactions which the adrenalines produce in detail, in individual organs and tissue units, when they are released at nerve endings to transmit the localized effects of adrenergic nerve impulses. There is no comparable secretion of acetylcholine as a hormone. It is in fact destroyed so rapidly by cholinesterase in the blood that its action through the general circulation would be extremely inefficient. For some years, the lack of chemical identification of acetycholine as a natural constituent of the body left even the exact nature of the cholinergic transmitter still open to question, so that many referred to it as an acetylcholine-like substance. However, the late H. W. Dudley and I came across it in 1929, when we were looking for something else, in the spleens of certain animals, and in quantities sufficient to enable us to isolate and identify it.

Another problem then soon began to present itself, namely, that of the physiological significance to be assigned to the other aspect of the action of acetylcholine, in which, like nicotine, it acts as a specific stimulant of the nerve cells in autonomic ganglia, and of the motor end-plates of voluntary muscle fibres. Was it possible that it was released at the synaptic nerve endings, as a chemical agent of the swift, unitary, impulse-for-impulse transmission of excitation to these structures also ? If so, it must be released there with a flash-like suddenness and then vanish almost as quickly, after starting the secondary impulse—from ganglion cell or motor end-plate—as a separate event. The weight of general tradition was heavily against any such interruption, at these synapses, of a continuous, electrical conduction by the interposition of such a chemical phase. Yet when, nearly 20 years ago, a group of which I was a member began to put its possibility to the test of direct experiment, the evidence in its favour began to accumulate quickly. When a sympathetic ganglion, or a voluntary muscle, was perfused with a suitably warmed saline solution containing a small amount of the protective physostigmine, acetylcholine appeared in the outflowing fluid when the preganglionic or motor nerve was stimulated, so that impulses arrived at the synaptic endings, but only then. Acetylcholine was still thus liberated at the synapses even if the ganglion cells or the motor endplates had been made insensitive to its action, as by curarine; but no excitation then passed across the synaptic junctions. On the other hand, a muscle deprived of its nerve-endings by degeneration still contracted vigorously when it was directly stimulated, but no trace of acetylcholine was then liberated.

FIGURE 2 – *Photomicrographs of motor nerve endings on end-plates of intercostal muscle fibres of rat. (Above) Stained by the Janus Green and ammonium molybdate method of Couteaux; (below) defined by a histochemical reaction, causing a deposition of copper sulphide where cholinesterase is concentrated. (Koelle, G. B. and Friedenwald, J. S.,* Proc. Soc. exp. Biol., N.Y., **70**, 617, 1949.)

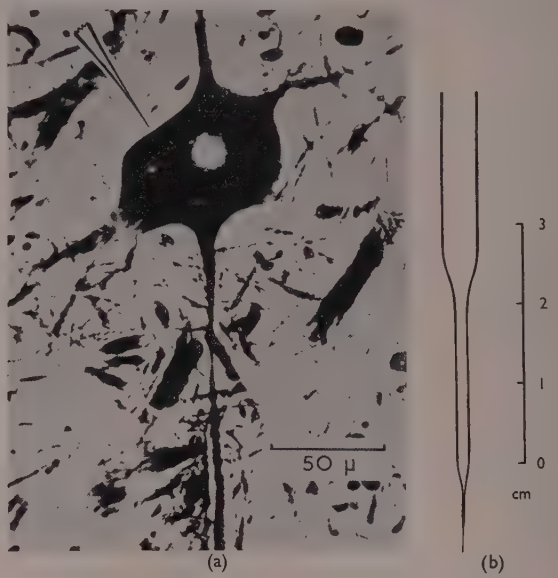


FIGURE 3 – (a) *Photomicrograph of cat spinal motoneurone and axone (pyridine silver stain), with superimposed tracing of microelectrode tip at same magnification to indicate small proportion of total cell surface which will be damaged by direct puncture.* (b) *Scale diagram to show form of Pyrex microelectrodes used. (Brock, L. G., Coombs, J. S., and Eccles, J. C.,* J. Physiol., **117**, 434, 1952.)

A chemical mechanism of this kind would obviously account for all the special characters of transmission across these junctions which we considered earlier; and, in more recent years, it has been supported, and elucidated in most convincing detail, by experiments carried out by some of those who, in the first instance, had reacted most strongly against it. Investigations still in vigorous progress make it possible already to describe the process of transmission from motor nerve-ending to muscle end-plate in much fuller detail. The motor end-plate responds to the arrival of an impulse at the nerve-ending by a relatively slow wave of depolarization, the end-plate potential, for which the only effective stimulus is the small quantity of acetylcholine liberated by the impulse at the nerve-ending and then vanishing quickly, partly at least through the action of a local concentration of cholinesterase at the nerve-ending, which can even be histochemically demonstrated (figure 2). When the end-plate potential has attained a sufficient level it initiates, and becomes masked by, a sudden reversal of polarity which then sweeps, as an electrically conducted impulse, in both directions along the main, contractile part of the muscle fibre. Physostigmine and its synthetic analogues (e.g. neostigmine), by depressing the cholinesterase at the nerve ending, prolong the persistence of the acetylcholine liberated by a nerve impulse and thus of the end-plate potential, so that a single nerve impulse then evokes a succession of conducted waves along the muscle fibre, producing a brief tetanus. Curarine, on the other hand, reduces the end-plate potential below the limit at which it is effective in starting the conducted wave; physostigmine then increases it again, by reducing the rate at which acetylcholine disappears (figure 4), and may even restore transmission if the curarization is weak. With differences of detail, an analogous sequence of events can be predicated for the synaptic transmission in a ganglion. Here, acetylcholine liberated at the synaptic nerve-endings causes a primary, relatively slow depolarization of the ganglion cell surface, which, when it reaches the effective potential, elicits a sudden reversal of polarity, starting an impulse which is then conducted by the usual electrical process along the post-ganglionic axone fibre.

Earlier evidence concerning the direct action of acetylcholine on voluntary muscle had not been of a kind to encourage belief in its function as transmitter of these effects of motor nerve impulses, each causing a single, rapid twitch of the muscle. Acetylcholine had merely been observed to cause

slow contractures of low tension when normal frog's muscles were soaked in weak solutions of it. It became clear, however, that we could not expect to imitate the response of a muscle to a volley of nerve impulses by an artificial application of the transmitter, unless the latter could be brought suddenly and simultaneously into contact with all the motor end-plates of the fibres. A much closer approximation to such a simultaneous application was achieved by suddenly injecting acetylcholine, in suitably small doses, directly and forcibly into the momentarily emptied arteries of the muscle; the contractions thus elicited were just of the kind —short, irregular bursts of tetanus—which acetylcholine ought to produce under these conditions, if it were indeed the transmitter of motor nerve effects.

Space is lacking for more than a passing mention of the practical applications already made, and still in rapid development, of the knowledge that transmission at these peripheral synapses is effected by the liberation of acetylcholine. The controlled use of curarine, and of synthetic substitutes for it, is now procuring for the surgeon a safe and reversible relaxation of the tone of the voluntary muscles. Agents of an allied type are used to block the transmitting action of acetylcholine at ganglion synapses, and thereby to lower the arterial pressure and secure a bloodless field of operation. The action of physostigmine, and especially of its synthetic analogues, is being used for the merciful reinforcement of a faulty nerve-muscle transmission in *myasthenia gravis*. On the other hand, the search for more and more potent antagonists of cholinesterase appears to be yielding, not only more active insecticides, but, alas, more threatening nerve poisons for the abuse of science in war.

There is one further and recent development which must be briefly mentioned. The functional analogy between the peripheral synapses in ganglia and muscles and those which form so essential a feature of the immense complexity of the grey matter of the central nervous system has long been obvious to all workers in this field. Many suggestive indications of a chemical transmission, in one part or another of the brain or spinal cord, had been obtained, but the investigators concerned had, in the main, been looking by different methods for evidence of a cholinergic transmission in particular, at the synapses of some central nuclei. Evidence in more general support of a chemical process has, however, recently come from an unexpected quarter. Professor Eccles, now of the Federal University at Canberra, had long opposed the idea of chemical transmission at the synapses in

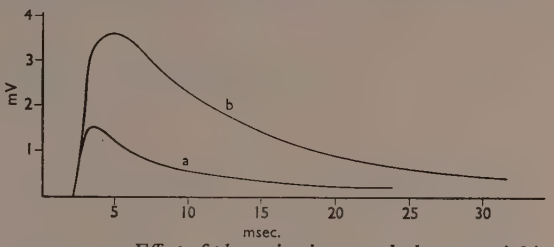


FIGURE 4 – *Effect of physostigmine on end-plate potential in fully curarized frog's sartorius (temp. 22° C)* (a) *after* 6μ *mols curarine;* (b) *after* 6μ *mols curarine + physostigmine* 1 *in* 10^5. (*Eccles, J.C., Katz, B. and Kuffler, S. W.*, Biol. Symp., 3, 364, 1941.)

autonomic ganglia. Recently, however, he and his colleagues have succeeded in inserting microelectrodes into single nerve cells of the ventral horns of the spinal cord—large motor cells (figure 3), the axones of which are the motor nerve fibres for voluntary muscle. From the changes of potential between the surface and interior of such a cell, which they have thus been able to record, and especially from the increase of the resting potential which they have found to accompany the synaptic transmission of an inhibitory effect, they conclude that chemical transmitters, excitatory and inhibitory for the particular cell, must be concerned in the process. To this it must be added that neither of the transmitters identified at the periphery can be one of those active here, since, from independent indications, it is clear that the fibres which conduct the impulses to these particular synapses are neither cholinergic nor adrenergic. Thus a promising field of further investigation here lies open.

It may be recalled, in this connexion, that there is no doubt that the motoneurone, with its axis cylinder forming a motor nerve fibre of which the endings make ultimate contact with the motor end-plates of voluntary muscle fibres, is cholinergic; we therefore have here a case of presynaptic nerve fibres which are not cholinergic making synaptic contacts with the cell body of a cholinergic neurone. The work of Feldberg and Vogt, in particular, who have explored different nuclei and fibre tracts of the central nervous system for the presence of the enzyme system producing acetylcholine, has led them to suggest that such an alternation of cholinergic and non-cholinergic neurones, in a chain linked by synapses, may be frequently found in the central nervous system. It is not, however, a constant arrangement, since the peripheral nervous system furnishes undoubted examples of the synaptic linkage of two cholinergic neurones in direct succession.

Stereochemistry: its basis and application to inorganic compounds

W. G. PALMER

The theory of the tetrahedral carbon atom, due to van't Hoff and Le Bel, long provided inspiration for the attack on certain problems of stereoisomerism, but it left many questions unanswered in the organic field, and proved misleading when applied to inorganic substances. Recent advances, however, both practical and theoretical, have permitted much progress to be made in our knowledge of interbond angles in many different elements. Neutron diffraction promises to provide a means of locating the hitherto elusive hydrogen atom.

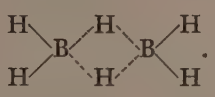
The subject of stereochemistry has never been expected to embrace the study of the actual shapes of molecules, and although we have today enough information to pursue such a study, it would prove to be one of extreme lengthiness. To identify the shape of a molecule composed of only two sorts of atoms, only the interbond angles are required. Thus SF_6, with all bond angles 90°, must be octahedral; SiF_4, with angles 109°, must be tetrahedral; while BF_3, with angles 120°, is obviously plane triangular. In general, however, molecular shape depends not only upon bond-angles but on bond-lengths: CCl_4 is certainly tetrahedral, but the shapes of the molecules CH_3Cl and CH_2Cl_2, also with tetrahedral angles, depend on the bond-lengths C—H and C—Cl. Just as the crystallographic constants of a substance are in general unique, so the shape of a molecule composed of more than two kinds of atoms cannot be exactly the same in detail as that of any other. In a chemical entity AX_n (X univalent), the angles subsisting between the bonds A—X seem to be determined almost exclusively by the properties of the central atom A, and often persist in spite of a wide variation in the chemical nature of the atoms X. Stereochemistry today, as originally in the conception of van't Hoff and Le Bel, is concerned with the study of such interbond angles, and particularly with how they are related to the nature and chemical state of the multivalent atom involved. In this sense we may logically refer to the stereochemistry of an atom, imposing itself on the molecules of which the atom forms a part.

To initiate the advances of recent years, two kinds of innovation were necessary: first, new practical methods capable of revealing the three-dimensional geometry of molecules in metrical terms; secondly, a convincing theory of why the bonds formed by multivalent elements preserve in general a rigid relative configuration in space, which is by no means always the most symmetrical disposition. So much has the situation been changed by the development of such methods and theories that today the problem is rather to escape embarrassment from the plenitude of results flowing daily from them. Space will permit little more than an enumeration of the new practical methods.

Methods	*Physical state of material examined*
A. Diffraction:	
of X-rays	Crystalline solids
of electrons	Gases and vapours at diminished pressure
of neutrons	?
B. Infra-red and Raman spectroscopy	Vapours, solutions, and solids
C. Measurement of dipole moment	Solutions and vapours

By far the greater part of our present stereochemical knowledge has been gained by the employment of diffraction methods. It will be seen that, in regard to the physical state of the material under analysis, the X-ray and electron methods are largely complementary. Physically the two methods differ, for while X-rays are scattered by atomic electrons, an electron beam interacts with nuclei, but both methods suffer from the defect that the spatial positions of atoms of small atomic number (light atoms) cannot usually be fixed in the presence of heavy atoms: the position of hydrogen eludes direct observation

in all circumstances—a serious drawback for the organic chemist. When it is fully developed, the method of neutron diffraction, still in its early infancy, is expected to counteract this defect. Second in power to diffraction methods come those of infra-red and Raman spectroscopy. Infra-red (absorption) spectra and Raman (emission) spectra arise directly from intramolecular vibrations. The number, spectral distribution, and character of the spectral bands are influenced mainly by the symmetry of the vibrating molecule. It is therefore a decision upon this latter molecular property that directly emerges from spectroscopic examination. Metrical results (bond-lengths and bond-angles) can be established with extreme accuracy for sufficiently simple molecules. Two examples of recent successes by the infra-red method, in which diffraction methods signally failed (for the reasons mentioned), are provided by iodine pentafluoride, IF_5, and diborane, B_2H_6. For the first compound the vibrational pattern demanded a square pyramid (see figure 11), and in the second the hydrogen bridges came clearly to light in the still problematical structure



The method of dipole moments is ancillary to methods A and B. Its results, from the stereochemical point of view, are nearly always qualitative. The existence of definite moments in H_2O, SO_2, and NH_3 proves the first two molecules to be triangular, and ammonia pyramidal: the moment of ozone shows that the classical structure O—O(O) is unacceptable. The method, however, fails to give actual bond-angles.

The new explanation of directed valency is implicit in the wave-mechanical theory of atoms and molecules, and can be understood only in the light of this conception, but to avoid too long a digression an outline of the theory is relegated to an appendix. Since, in the modern theory, wave-functions Ψ replace the electronic orbits of classical theory, they are commonly termed orbitals. They can in general be expressed as a product of axial function and radial function, that is as $[\varphi(x, \ldots)][f(r)]$, where r is a point lying anywhere upon a sphere of radius r round the centre of the atom, and x, y, and z are rectangular axes with origin at the centre of the atom. Orbitals are 'equivalent' when they have the same algebraic form but are associated with different axes. To illustrate the interpretation of a wave-function Ψ we may consider a p type of orbital, say p_x, of the form $x.f(r)$, indicated graphically in figure 1(*a*). This orbital has yz as a plane of symmetry, and is clearly axially symmetrical round x, so that the figure is really a sectional view. We may legitimately expect Ψ to present information about the position of the electron in the atomic system, about which we know *a priori* two facts, with which p_x harmonizes: the electron neither falls into the nucleus, nor recedes indefinitely away from it. The difficulty that (as may be expected of a quantity that is essentially an amplitude) p_x changes sign at the atomic centre is resolved by considering Ψ^2 instead of Ψ. The accepted meaning of the statement 'an electron is in the orbital p_x' is as follows:

1. The position of the electron in the atom is expressible only as a probability, measured by Ψ^2. This property is fundamental to all wave-functions.
2. The most probable location of the electron is along the axis x, with two equal maxima at the points e (figure 1(*a*)).
3. There is no chance whatever that the electron is located along the directions y or z.

An exactly similar interpretation may be given for $p_y = y.f(r)$ and $p_z = z.f(r)$, with suitable exchange of x for y or z. Thus if the orbitals p_x, p_y, and p_z each contain one electron, each electron may be regarded as essentially confined to one of the mutually perpendicular axes x, y, or z.

In spite of the promising form of directed orbitals such as those of the p and d kind, we have not yet quite reached the stage at which the theory can assist in interpreting stereochemical facts. In bivalent beryllium, the valency electrons are held respectively in an s and a p orbital

Atomic orbitals			
Spectroscopic nomenclature	*Radial function*	*Axial function*	*Number of equivalent orbitals*
s	$f_s(r)$	$x^0 = y^0 = z^0 = 1$	1
p	$f_p(r)$	x, y, z	3
d	$f_d(r)$	x^2, y^2, z^2 xy, yz	3 2

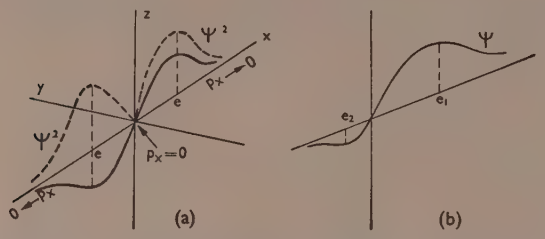


FIGURE 1 – *Representations of atomic wave-functions ('orbitals'). (a) An orbital of the* p *type. (b) A mixed or bonding orbital.*

(configuration *sp*): in tervalent boron the configuration is sp_2, that is *s*, p_x, and p_y. In both atoms, each valency electron has nearly the same total energy, since the *s* and *p* orbitals belong to the same (*L*) shell. Hence the functions *s* and *p* for Be, and *s* with p_x and p_y for B, are solutions of wave-equations of nearly identical form. A short consideration of the general wave-equation will show that, for beryllium, functions such as $\Psi_1 = s + p$, or $\Psi_2 = s - p$ satisfy the equation equally with the simple functions. When the spatial properties of Ψ_1 and Ψ_2 are worked out we find that, in common with *p* orbitals, they are equivalent, have axial symmetry, have a node near the atomic centre, and rapidly decrease to zero in outward directions, as all true wave-functions must do. The axes of Ψ_1 and Ψ_2 are, however, separated by 180°, i.e. they are collinear, but the most important distinction from *p* and other simple atomic orbitals lies in the position of the maximal points *e*, and in the large difference between the values of Ψ^2 at these points (figure 1(*b*)). While simple orbitals are always symmetrical about one or more planes through the atomic centre, Ψ_1 and Ψ_2 are very unsymmetrical about the nodal point, and there is a maximal chance much greater than that in a *p* orbital at points *e* (figure 1(*a*)) of finding the electron further from the nucleus and along only one side of the axis of symmetry (e_1, figure 1(*b*)). Colloquially we may say that it sticks out from the atom along the axial direction. Now this is just the sort of condition needed for the formation of strong chemical bonds with other atoms, since chemical union occurs when the orbitals of two atoms, each with its own electron, overlap spatially. However, as atoms approach each other to accomplish this overlap more and more extensively, the strong repulsion of their charged nuclei also constantly increases, and finally limits the closeness of approach. It follows that strong bonds will be formed only if sufficient overlap can be secured before the nuclear repulsion rises to prohibitive levels: for the strongest bonds the maximal point (such as e_1 in figure 1(*b*)) must lie as far from the nucleus as possible.

In a similar way, the orbitals sp_2 in boron can be made to yield three equivalent functions directed along axes mutually at 120°, and all co-planar: again the maximal point is in a more favourable position than in simple p_x or p_y. We might say that, as a consequence of mixing, the undirected *s* orbitals have been consumed by the resulting directed mixed orbitals. It cannot be too strongly emphasized that these derived solutions of the wave-equation are just as authentic as the original functions, and from the atomic wave-equations in themselves we can obtain no guidance about which orbitals will in fact be adopted when beryllium and boron form compounds. This uncertainty is removed when we recognize that an atom will always tend to form the strongest possible bonds, and these are evidently produced by using the mixed orbitals. The argument is confirmed by the observed facts that the atoms in $BeCl_2$ (and in $HgCl_2$) are collinear, and that in boron compounds such as BF_3, BCl_3, $B(OH)_3$, and $B(CH_3)_3$ the atom of boron lies at the centre of an equilateral triangle and is co-planar with the centres of the combined atoms.

This principle of mixed orbitals operates also for elements of Group 5 (N, P, and As) and Group 6 (O, S, and Se), in the atoms of which, when in their lowest valency states (III and II respectively), not all the electrons in the valency shell are employed in forming bonds. In these atoms, the four simple orbitals which could be occupied are sp_3, which when submitted to the mixing process yield, as always, an equal number of orbitals, which in this case are equivalent and directed along axes mutually inclined at 109°, the

Bond angles in compounds of elements in Groups 5 and 6

Oxygen:		Nitrogen:	
OH_2	105°	NH_3	108°
$O(CH_3)_2$	111°(3°)	NH_2CH_3	108°
OF_2	105°(5°)	$N(CH_3)_3$	108°
OCl_2	111°(2°)	NF_3	103°
Sulphur:		Phosphorus:	
S_8	105°	$P(CH_3)_3$	101°(3°)
SCl_2	103°(3°)	PF_3	104°(4°)
S_2Cl_2	105°(5°)	PCl_3	101°(2°)

(*The probable error in the observations, when known, is given in parentheses.*)

tetrahedral angle. If we label these orbitals t_{1-4}, the electronic configuration for bond-formation is $t_1^2[t_{2-4}^3]$ in group 5, and $t_1^2t_2^2[t_{3-4}^2]$ in group 6. In these symbols the bonding orbitals, each occupied by a single electron, are enclosed in brackets, and the electrons in the orbitals are indicated by the upper indices: the valency of the configuration is therefore given by the upper index in the bracket. It will be noticed that, while the mixing of orbitals leads to stronger bonds, it cannot alter the valency. For convenience, in the sequel we shall indicate mixing by parentheses; thus $t_{1-4} = (sp_3)$.

It is a plausible proposition that, if mixing is to be considered at all, it should be confined to those atomic orbitals which are singly occupied by electrons. It can be shown that equivalent orbitals undergo mixing without change in properties: that is,

$$s, p_3 = s(p_3) = sp(p_2),$$

and the bond-angles of the compounds shown in the above table should be 90° instead of close to 109° as they actually are. It is essentially the inclusion of the (undirected) s orbital which brings the angle to the larger value.

Elements of the B families of groups 5, 6, and 7 (P, As; S, Se, Te; Cl, Br, and I), when exerting respectively the valencies V, IV, and III, all use a mixture of the five simple orbitals sp_3d, which, unlike the sets we have previously considered, cannot be made to give (five) equivalent orbitals, but yields directions pointing to the corners of a triangular bipyramid (figure 2). Clearly the polar directions are not geometrically equivalent to the equatorial directions. Probably for this reason, the mixed halides of phosphorus are all of the form PX_2Y_3, e.g. PCl_2F_3; PX_4Y and PXY_4 have not been obtained. If we call the mixed orbitals v_{1-5}, and indicate the bond-forming orbitals as before, we have:

Group 5 ..	$[v_{1-5}^5]$	Valency V
Group 6 ..	$v_1^2[v_{2-5}^4]$	Valency IV
Group 7 ..	$v_1^2v_2^2[v_{3-5}^3]$	Valency III

As examples of these configurations we show the

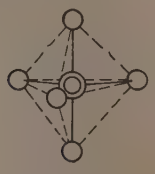


FIGURE 2 – *Phosphorus pentahalides: ◎, P; ○, halogen.*

FIGURE 3 – *The molecule PCl_2F_3: ◎, P; ○, Cl; ●, F.*

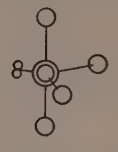


FIGURE 4 – *Tellurium tetrachloride, $TeCl_4$: ◎, Te; ○, Cl; ∞ electron-pair.*

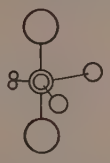


FIGURE 5 – *The molecule $Se(C_6H_5)_2Cl_2$: ◎, Se; ○, C_6H_5; ○, Cl; ∞ electron-pair.*

FIGURE 6 – *The molecules BrF_3 and ICl_3: ◎, Br or I; ○, F or Cl; ∞ electron-pairs.*

FIGURE 7 – *The fluoiodate anion $(IO_2F_2)^-$: ⊙, I^+; ○, F; ◎, O^-; ∞ electron-pair.*

three-dimensional structures of PX_5, where X is F, Cl, or Br (figure 2); of the mixed halide PCl_2F_3 (figure 3); of $TeCl_4$ and $Se(C_6H_5)_2Cl_2$ (figures 4 and 5); and lastly of the compounds BrF_3 and ICl_3 (figure 6). Of these structures, only those of the interhalogen compounds await experimental confirmation. The structures of phosphorus pentahalides, revealed by electron-diffraction, are those of the free molecules in the gaseous phase. On condensation to the crystalline state a remarkable structural reorganization takes place, which is discussed later. The unusual one-sided molecules containing Se(IV) and Te(IV) could hardly have been foreseen in classical stereochemistry, which would undoubtedly have assigned them a tetrahedral shape. It is unfortunate that there appear to be no analogous compounds of S(IV) sufficiently stable for experimental examination. Sulphonium salts of the form $(Sabc)^+.X^-$, in which the cation is enantiomorphic, were formerly relegated to the chemistry of quadrivalent sulphur, but since S^+, to which the groups a, b, and c are bound, is isoelectronic with phosphorus, the stereochemistry is essentially that of P(III), based on (sp_3). The cation is therefore pyramidal, like $P(CH_3)_3$, and the enantiomorphism is explained. The fluoiodate anion, $(IO_2F_2)^-$, the observed form of which is shown in figure 7, is an analogue of $TeCl_4$, since I^+ and Te are isoelectronic. The linear form of the ions $(ICl_2)^-$, $(IBr_2)^-$, and I_3^- also derives from the mixture (sp_3d), acting in the valency configuration $v_1^2v_2^2v_3^2[v_{4,5}^2]$. The assignment of the non-bonding orbitals v_{1-3} to the equatorial directions is a consequence of the equivalence of these (figure 8).

We come now to the bonding orbitals formed

by mixture of the six-fold set sp_3d_2, which, excepting only (sp_3), is the most frequently encountered in stereochemistry. The mixed orbitals, which we shall label o_{1-6}, are all equivalent, and have their maximal points along axes directed to the corners of an octahedron; all bond-angles are therefore 90°. This electronic configuration is found in the elements of group 6 when exerting their highest valency, and in a very large number of complex ions of the most diverse composition, such as $(SiF_6)^{2-}$, $(Fe(CN)_6)^{4-}$, $(Co(NH_3)_6)^{3+}$, etc. The octahedral forms of SF_6, SeF_6, and of telluric acid, $Te(OH)_6$, are indicated in figure 9. The anion of the para-periodates $(IO_6)^{5-}$, provides another example (figure 10), for, as mentioned above, I^+ is isoelectronic with Te. Further interesting examples, also from the stereochemistry of iodine, are found in the pentafluoride, IF_5, and in the anion $(ICl_4)^-$. Without the guidance of wave-mechanical theory and the experimental confirmation of its truth for the pentafluoride (figure 11), this compound would undoubtedly have been assigned a structure similar to that of the pentahalides of Group 5. Its square-pyramidal form in fact arises from the valency configuration $o_1^2[o_{2-6}^5]$, while that of the ion $(ICl_4)^-$ originates from $o_1^2o_2^2[o_{3-6}^4]$. The two non-bonding orbitals are naturally assigned to polar directions to minimize the repulsion of their electron-pairs (figure 12). It might be asked why a similar assignment to polar positions should not be found in the constitution of the ions ICl_2^-, etc., shown in figure 8. It appears that in this case the issue is decided by the logical principle that chemically identical

FIGURE 12 – *The anion* $(ICl_4)^-$: ◎, I^-; ○, *Cl; electron-pairs.*

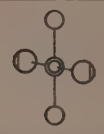


FIGURE 13 – *Cupric chloride dihydrate,* $CuCl_2.2H_2O$: ◎, *Cu;* ○, *Cl;* ◑, *O of* H_2O.

groups, such as the fluorine atoms in PCl_2F_3 or the three pairs of electrons in ICl_2^-, should be bound by equivalent orbitals.

It has been shown, by X-ray diffraction, that crystalline phosphorus pentachloride and bromide are formed of the ions $(PCl_6)^-$ with $(PCl_4)^+$, and $(PBr_4)^+$ with Br^- respectively. The essential constitution of cations $(PX_4)^+$ is properly expressed by $(P^+)X_4$, and that of $(PX_6)^-$ by $(P^-)X_6$. Now P^+ is isoelectronic with Si, and uses (sp_3), while P^- is isoelectronic with S and uses (sp_3d_2). Hence we predict a tetrahedron for $(PCl_4)^+$ and an octahedron for $(PCl_6)^-$, which are in fact clearly revealed in the crystal structure. It is possible that this remarkable change on crystallization reflects the preference of atoms to use orbitals all of which are equivalent, as in (sp_3) and (sp_3d_2), rather than those such as (sp_3d) utilized in gaseous PCl_5, which contain two sets of orbitals.

Finally we may touch upon the stereochemistry of atoms in complex compounds. It is well known that by far the commonest co-ordination numbers are 4 and 6. In complexes based on the latter the bonding orbitals are, in almost all cases, o_{1-6}, although there are a few exceptions to this rule.

FIGURE 8 – *The anions* $(IX_2)^-$: ◎, I^-; ○, *Cl, Br, or I;* ∞ *electron-pairs.*

FIGURE 9 – *The octahedral configuration of sulphur and selenium hexafluorides,* SF_6 *and* SeF_6, *and telluric acid,* $Te(OH)_6$: ◎, *Se or Te;* ○, *F or OH.*

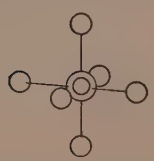


FIGURE 10 – *The anion* $(IO_6)^{5-}$: ◎, I^+; ○, O^-.

FIGURE 11 – *Iodine pentafluoride,* IF_5: ◎, *I;* ○, *F;* ∞ *electron-pair.*

Summary of the principal bonding orbitals

Orbitals combined	*Bonding orbitals*	*Valency angles*	*Occurrence*
s,p	(sp)	180°	Group 2
s,p_2	(sp_2)	120°	Group 3
s,p_3	t_{1-4}	109°	Group 4
	t_{2-4}	..	Group 5 (III)
	t_{3-4}	..	Group 6 (II)
s,p_3,d	v_{1-5}	120°, 180° 90°	Group 5 (V)
	v_{2-5}	..	Group 6 (IV)
	v_{3-5}	120°	Group 7 (III)
s,p_3,d_2	o_{1-6}	90°	Group 6 (VI)
	o_{2-6}	..	Group 7 (V)

While 4-coordination is very commonly based on $t_{1-4} = (sp_3)$ and is therefore tetrahedral, in the complexes of the bivalent ions of copper, nickel, palladium, and platinum the mixture (sp_2d) appears, which is not known to be associated with the primary valency of any atom. The orbitals are equivalent, and are directed to the corners of a square, so that all five united atoms are co-planar. This arrangement dominates the stereochemistry of the complexes of Cu^{2+}, and is well seen in $(Cu.\ 4NH_3)^{2+}$ and in cupric chloride dihydrate, $CuCl_2.2H_2O$, which is a wholly covalent structure (figure 13).

APPENDIX

In X-ray diffraction any two of the quantities (i) the wavelength λ_x, (ii) the crystal spacing d, and (iii) the angle of diffraction θ, determine the third. Today, the diffraction is used to find d, by measuring θ given by radiation of known wavelength λ, but originally the interest lay in determining λ. A beam of fast-moving electrons (which are particles of atomic weight 0·00055) suffers diffraction by crystalline matter in like manner, and again we can calculate λ_e for known values of d and observed values of θ. If the electrons have traversed a potential difference of P volts, the (kinetic) energy T_e of each on undergoing diffraction is P electron-volts. Whatever meaning we may attach to λ_e, experiment shows that the relation

$$(\lambda_e)^2 = (\text{constant})/P = (\text{constant})/T_e$$

is precisely obeyed. It may be remarked that this power of varying λ_e by merely altering P gives to electron-diffraction a flexibility lacking in that of X-radiation: in practice, for $\lambda_e \sim 10^{-8}$ cm, P is of the order of 100 volts. Stating a wavelength is only a short way of saying that the amplitude Ψ of the wave varies periodically. For a wave moving in the direction x, such variation is expressed in the equation (for X-radiation)

$$(\text{constant})\frac{d^2\Psi_x}{dx^2} = -\frac{1}{\lambda_x{}^2}\,.\,\Psi_x.$$

For electrons we may therefore presumably expect the relation

$$(\text{constant})\frac{d^2\Psi_e}{dx^2} = -\,T_e\,.\,\Psi_e.$$

Herein interest is shifted from λ_e to an amplitude Ψ_e—as we have seen, advantageously.

In chemistry, and especially in stereochemistry, we are interested not in the properties of electrons freely moving in space but in those of electrons bound, with potential energy V, in an atom or molecule. For a hydrogen atom $V = -e^2/r$, where r is the distance of the electron from the singly charged nucleus. For an electron thus confined, the total electronic energy will be $E = T + V$, and we must assume that T and V will both vary with the position of the electron, while E remains constant. Further, we can no longer be satisfied with only one spatial variable. For a bound electron, then, we write

$$(\text{constant})\left[\frac{d^2\Psi}{dx^2} + \frac{d^2\Psi}{dy^2} + \frac{d^2\Psi}{dz^2}\right] = -\,(E - V)\Psi.$$

Since in stereochemistry we are concerned with the algebraic form of Ψ and not with its absolute magnitude, we may set the constant arbitrarily as equal to unity, and write finally

$$[V - \nabla^2]\Psi = E\,.\,\Psi,$$

where ∇^2 represents $\dfrac{d^2}{dx^2} + \dfrac{d^2}{dy^2} + \dfrac{d^2}{dz^2}$. It will be seen that the forms of Ψ (which will be functions of x, y, and z) that satisfy this equation must, when submitted to the mathematical operations specified in the bracket, be reproduced unchanged, except for multiplication by a constant E. This exacting requirement means that such wave-functions Ψ are very limited in number, and in consequence the total energy E can take only a limited number of values. In short, our wave-equation predicts directly the long-known stationary states of an atom, which up to the time of the discovery of wave-mechanics remained entirely inexplicable. The equation may, by the aid of standard methods, be solved for the hydrogen atom $(V = -e^2/r)$, but it is much more difficult to obtain solutions for more complicated atomic systems. Fortunately, it may be shown that those general properties of the solutions for hydrogen, used in the foregoing discussion, are applicable to atoms in general.

Guillaume-François Rouelle (1703–70)

DOUGLAS McKIE

In science, as in other fields of learning, the inspiring teacher can often exert as fertile an influence as the contributor of new knowledge. It is as a great teacher of chemistry that Rouelle is chiefly remembered, a man who numbered among his pupils almost all the leading French chemists of the latter half of the eighteenth century. Rouelle bridged the gap between the old chemistry and that arising from the chemical revolution which culminated in the work of Lavoisier. Moreover, he found time to make original chemical discoveries.

As the great intellectual movement inspired by the *philosophes* of eighteenth-century France gathered momentum, there began to appear, under the editorship of Diderot and d'Alembert, the first volumes of the *Encyclopédie*, in which the beliefs and ideas of these reformers and their criticisms of current thought and contemporary society were set forth. The third volume was published in 1753 and contained an article on chemistry by Venel (1723–75), professor at Montpellier, the text of which bears evident signs of having been edited by Diderot. After stating that chemistry received little attention in France, the writer asserted: 'This science is only indifferently studied even by natural philosophers, despite the pretensions to universal knowledge that are nowadays fashionable. The chemists, moreover, are a class apart, few in numbers, having their own language, their laws, their mysteries, living almost in isolation amidst a great nation and with scant curiosity about its commerce and no thought for its industry.' But a change must be hoped for: 'The revolution that would raise chemistry to the position that it deserves, and that would place it at least alongside the exact science of physics, can be expected only at the hands of a chemist who is at once a skilful experimenter and an enthusiastic and fearless thinker.'

Three years later, in 1756, Francis Home (1719–1813), professor in Edinburgh, was complaining that chemistry 'has been for many years too tame and confined. It seldom ventures further than the composition of a medicine, as if that were all the service it could be of to mankind.' At this date, Joseph Black's researches on *magnesia alba* had just been published, and Lavoisier was a schoolboy of thirteen.

In the 1750's, therefore, French and British minds had reached a common conclusion and were united in their lamentations about the state of chemistry.

Some twenty years later still, Diderot was invited by the Empress Catherine II of Russia to advise her on education in general. In a long and detailed document, he dealt with the various subjects to be studied. When he came to chemistry, he made three points. First, he emphasized the usefulness of this science. Secondly, he quoted, with evident relish and adding that he felt that the opinion was not in any way unjustified, the comment of Becher (1635–82), originator of the phlogiston theory, that 'physicists were merely so many stupid animals who licked the outsides of bodies.' Thirdly, he recommended that the lecture notebooks of Rouelle, which had been revised, corrected, and enlarged by Rouelle's brother and d'Arcet, should be acquired and used for the teaching of chemistry and its application to the mechanical arts. When Diderot formulated his report, however, the revolution in chemistry was already under way and within some ten years or so of its completion; but his recommendation about Rouelle's notebooks was a deserved tribute to an inspiring teacher, who had done more for chemistry in France than any of those who had preceded him, and who had numbered among his pupils almost all the French chemists of the second half of the eighteenth century, including Macquer, Bayen, Venel, Cadet, d'Arcet, Roux, Bucquet, Leblanc, Proust, and, not least, Lavoisier. There had been great teachers of chemistry before Rouelle, especially Lemery in France and Boerhaave in Holland; and, before Rouelle died, Black's teaching was renowned throughout Europe. Nevertheless, Diderot's judgment was soundly based. Today, the historian of chemistry would place Rouelle, so far as France is concerned, between the old and the new, and recognize him as the link between the ancient ways of chemistry and the new chemistry of Lavoisier.

Guillaume-François Rouelle was a Norman, born in 1703 at Mathieu, near Caen, into a farming family. At his school, the *Collège du Bois*, at Caen, he gave early promise of much greater interest in science than in literature: he collected

FIGURE 1 – *Guillaume-François Rouelle* (1703–70), *demonstrator in chemistry at the* Jardin du Roi (1742–68), *member of the* Académie des Sciences (1744), *and teacher of Lavoisier.* (*Reproduced from a miniature, artist unknown, by kind permission of the Science Librarian, Clifton College, Bristol.*)

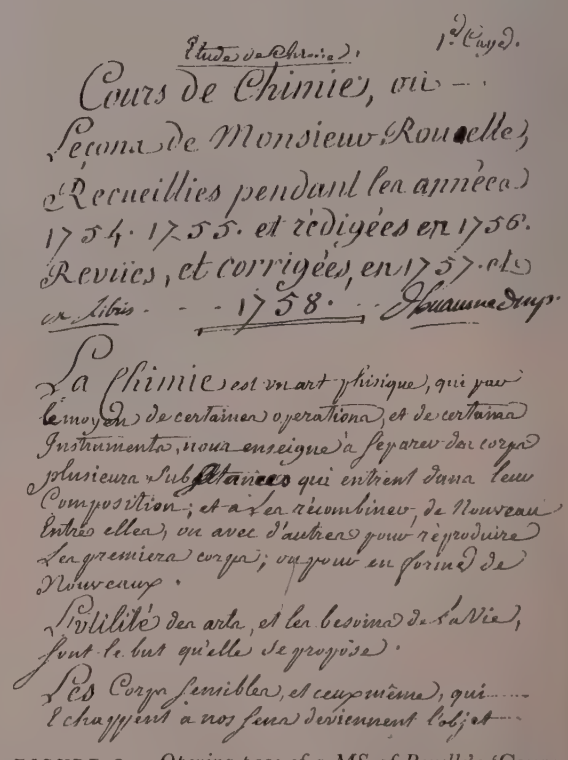
mineral and botanical specimens and cultivated a small garden of rare and curious plants. On leaving school, he entered the University of Caen to study medicine; but, disliking dissection and unable to discipline his sensitive mind in the presence of suffering, he abandoned the hope of becoming a physician and turned his attention to chemistry, for which he had always had a strong enthusiasm. His improvised laboratory consisted of the smithy of a neighbouring brass-worker with its forge, furnaces, and utensils, and he even gathered some pupils around him. Presently, in 1725, he left for Paris to carry his studies further, accompanied by two friends whom he had inspired with a taste for science. Not wishing to abandon medicine altogether, Rouelle decided to study pharmacy, the branch of medicine that had most connexion with his favourite science of chemistry. Accordingly, he found a place with a German apothecary, Spitzley, with whom he spent seven years, greatly extending his knowledge, both by experiments and by reading, and also by his contacts with many of the leading French scientists of that time. Afterwards he set up for himself in the *Place Maubert*, where he gave courses in chemistry and pharmacy, which proved so attractive as to command large audiences anxious to be instructed by an interesting and lively personality, and which led to his appointment as demonstrator in chemistry at the *Jardin du Roi* in 1742.

Here, from 1742 to 1768, Rouelle not only taught but popularized chemistry; his audiences included scientists, writers, gentlemen of the court, ladies of fashion, students, and others, to all of whom he communicated his enthusiasm. By practice long established at the *Jardin du Roi*, the lectures were given jointly by the professor and the demonstrator. The professor gave a discourse and was followed by the demonstrator, whose duty it was to provide experimental evidence of the

ideas and theories that the professor had expounded. Rouelle's professor was Bourdelin, a cold and formal speaker, who customarily ended his lecture with the announcement: 'Such, gentlemen, are the principles and the theory of this operation, as the demonstrator will now prove to you by his experiments.' However, Rouelle mostly did the very opposite and disproved the professor's theories, and his method of lecturing added a piquancy to his criticisms. He would begin calmly; but he was neither a restful character nor a fluent speaker, and often he was not grammatical, but, as he said, he was not teaching at a school of elocution, and he soon warmed to his work. In his difficulty in expressing his thoughts, he would appear momentarily stifled. He arrived in the lecture-theatre in full dress, but when the words would not come, off went his hat, which he sometimes hung on a retort; then in turn off came the wig, to be hung on some other piece of apparatus, and then the cravat, followed by the velvet coat and after it the velvet waistcoat. Speech was now easier, and a torrent of facts and ideas poured forth, Rouelle rapidly striding to and fro as he spoke. With him was his nephew, whose task was to bring forward in readiness the apparatus that his uncle would need at various points of an apparently unrehearsed discourse. The unfortunate assistant, however, never knew where Rouelle's restless thought or his restless limbs would carry him, and the apparatus was rarely ready at the time and place required. Momentarily interrupting himself to protest 'Nephew, where are you? You nuisance!' Rouelle, resuming his lecture, would continue speaking while going to the laboratory at the back of the theatre to get the apparatus that he required. On his reappearance, he had usually completed what he had been saying, and often he concluded with the words, 'Well, gentlemen, that is what I had to say to you.' But, if asked, he would willingly repeat the demonstration, as if his audience had not correctly grasped it. Occasionally there were explosions, the theatre was filled with fumes, and the audience precipitated themselves through the windows into the garden. Sometimes, Rouelle would express a completely new idea or describe some new process, which he would prefer to have kept to himself, and then would say: 'That is one of my secrets which I tell to nobody.'

His lectures were interspersed with criticisms of, and quips against, his scientific contemporaries, even while they were present listening to him. Macquer and Buffon were often greeted with these sallies: the worst term in his armoury of abuse was 'plagiarist,' and it was the final word. Every year at a certain point in his lectures, speaking of Bordeu, the physician, he would add: 'Yes, gentlemen, that's one of our people, there he is, a sawbones, a plagiarist, who killed my brother.' It says much for Rouelle's character and personality that none of his victims took offence at his diatribes. Diderot frequently attended Rouelle's course and took careful notes: a set of these notes came into the possession of Lavoisier, who studied them closely when he attended the lectures himself, probably in 1763–4.

In 1744 Rouelle was elected to the Academy of Sciences in the grade of assistant, and in 1752 was promoted to associate. Between 1744 and 1754 he published five memoirs in the Academy's annual volumes of *Mémoires*. The most important of these dealt with the problem of the nature of salts, and contained Rouelle's classic contribution to chemical philosophy. His views are best appreciated by the modern reader if it is first understood that the term base was only then coming into


Cours de Chimie, ou —
Recueillies pendant les années
1754. 1755. et rédigées en 1756.
Revues, et corrigées, en 1757. et
1758.

La Chimie est un art physique, qui par
le moyen de certaines operations, et de certains
Instruments, nous enseigne à separer des corps
plusieurs substances qui entrent dans leur
Composition; et à les réunir de nouveau
entre elles, ou avec d'autres pour reproduire
les premiers corps; ou pour en former de
Nouveaux.

L'Utilité des arts, et les besoins de la Vie,
sont le but qu'elle se propose.

Les Corps sensibles, et ceux même, qui
échappent à nos sens deviennent objet —

FIGURE 2 – *Opening page of a MS of Rouelle's* 'Cours de Chimie,' *taken down from his lectures in* 1754–5 *and revised from the lectures given in* 1756, 1757, *and* 1758. *The MS runs to over a thousand pages.* (*Reproduced by kind permission of the Science Librarian, Clifton College, Bristol.*)

use in our modern sense. To Rouelle, a salt was a solid substance produced by the combination of an acid with a base. He recognized the existence of neutral salts, as he called them, which we now call normal salts, in which acid and base were exactly saturated by one another. Their neutrality was demonstrated by the fact that they did not change the colour of an indicator then in common use, namely syrup of violets. Further, he recognized acid salts, containing in combination, and not merely admixed, a proportion of acid beyond that in the neutral salt. Besides these, there were also salts with the minimum proportion of acid: they included, for instance, silver chloride and calomel, but Rouelle advanced chemical theory in considering these substances as salts, since they had not previously been so regarded because of their slight solubility. He did not arrive at the idea of basic salts, but he had made a great step forward in his definition and his classification of salts, and his work has contributed to what we accept today.

While demonstrator at the *Jardin du Roi*, Rouelle continued his courses in the *Place Maubert*, but in 1746 he moved to the *Rue Jacob*, near *La Charité*, where he enlarged his laboratory by a dispensary in 1750, in which year he was elected to the Royal Academy of Sciences of Stockholm and to the Electoral Academy of Erfurt. In 1768, in bad health, he resigned from his post at the *Jardin du Roi*, and he died at Passy on 3rd August, 1770. After his death, efforts were made to edit and publish his lectures. Various sets of notes were collected by his brother, Hilaire Marin (1718–79), who succeeded him at the *Jardin du Roi*, and by d'Arcet, and were carefully collated, but the project was never completed. Several of these MS lecture notebooks have survived: the present writer is pleased to express his gratitude to the Science Librarian, Clifton College, for access to one of them—a very fine copy, from notes originally taken down in 1754–5, which were re-edited in 1756, and revised and corrected in 1757–8 from Roux and d'Arcet's copy of Rouelle's lectures during these years.

Before summarizing the contents of some of the surviving manuscripts, it needs to be emphasized that it was Rouelle who introduced the phlogiston theory into France. Much has been said for and against the phlogiston theory, as of all discarded and outworn systems; it was, however, the first great generalization in chemical philosophy, and it brought chemistry away from the alchemist and the apothecary. It is not surprising, therefore, that Rouelle's contemporaries regarded him as the founder of chemistry in France.

The manuscript notebooks show that Rouelle defined chemistry as the art of separating bodies into their various component substances and of recombining these products to give either the original substances or new ones: it was a science, he said, that sought for facts, not vain arguments, and it was concerned with the useful arts and human needs. He accepted the four-element theory of earth and air, fire and water, though fire he replaced by phlogiston; and he thought that there might be a fifth element, the 'mercury' of Becher. But it was not these elements that combined to form compounds, but various combinations of them, about ten or twelve in number, which then combined with one another. It was by the transfer of an element from one compound to another in chemical change that its properties were discovered. The elements were indestructible, immutable, indecomposable. The general descriptive matter was arranged according to the vegetable, animal, and mineral kingdoms, but Rouelle thought that there were three other kingdoms—watery, earthy, and aerial. Contemporary knowledge was well expounded in this systematic way, and there was an extensive account of chemical apparatus and its uses, especially for the process of distillation. Rouelle was familiar with the work of Boyle and of Hales on air, and he considered that 'air' entered into the composition of bodies. In his demonstrations he used a modified form of Hales' pneumatic trough to collect and measure the 'air' obtained by heating a variety of substances. It must have been in this form of apparatus that Lavoisier first witnessed the collection of an 'air.' Rouelle thought that air owed all its mobility to the fire contained in it, and that, this being removed, air would assume a concrete form. In his general discussion he held that volcanoes were due to masses of water penetrating fissures in the earth's surface and meeting with internal fires, and that it was not possible to doubt the origin of fossils in sedimentary rocks or to imagine that they were sports of nature. Rains and rivers were continually eroding the earth's surface as the sea eroded the coasts. The preparation of the mineral acids was described and also that of their salts, and crystal forms were studied. As for alchemy, Rouelle considered that judgment ought to be suspended, since so many reputable writers had stated that they had observed transmutations, but said that he would like to witness one himself in order to settle some doubts that still remained in his mind.

The evolution of adaptations

C. H. WADDINGTON

Current biological belief regards evolution as being primarily the result of the natural selection of random mutations, useful adaptations gradually spreading throughout a race. Professor Waddington regards this as an extreme view, and in this article puts forward a hypothesis to explain how acquired characteristics may become hereditarily fixed by a process of genetic assimilation not invoking the generally discredited theory of direct inheritance.

It is abundantly found in the living world that the structure of an animal or plant is very precisely adapted to the functions which it has to perform. The nature of the processes by which this situation has been brought about during evolution provides one of the major problems for biological theory. The hypothesis of the inheritance of acquired characters suggested that in some way or other the effects of functioning become themselves inherited. It has usually been interpreted to mean that the reaction between the organism and its surroundings has, as one of its results, an effect on the germ-plasm such that new hereditary changes occur, of a kind which determines the development in later generations of individuals suited to these particular conditions of life. Although this idea has recently been revived in a rather nebulous form in the Soviet Union, it has been so completely rejected by the rest of the scientific world that it is hardly considered to be worthy of discussion in most of the important recent works on evolution. The reigning modern view is that, in nature, the direction of mutational change is entirely at random, and that adaptation results solely from the natural selection of mutations which happen to give rise to individuals with suitable characteristics. I want to argue that this theory is an extremist one, and that, in essaying to account for adaptation, it neglects to call to its aid the doctrines emerging in other fields of modern biology which can quite properly be combined with the conclusions of genetics in the strict sense. In the discussion which follows, attention will be confined to animals, but there is no reason to doubt that similar arguments could be advanced in the botanical field.

It will be advisable first to glance briefly at the phenomena which are usually referred to under the heading of adaptation, since they are of several different kinds which must be distinguished from one another.

There is, first, a category in which an animal living under particular circumstances, or behaving in a particular way, itself becomes modified so as to be better fitted for its special circumstances. Examples of such 'exogenous' adaptations are legion. If muscles are continually and intensely used, they become thicker and stronger; if one kidney is removed from a mammal, the other hypertrophies; if the forelegs are absent at birth, or removed shortly afterwards, from rats or dogs, the hind-limbs become modified to suit the bipedal gait which the animals are forced to adopt; if skin is subjected to frequent rubbing and pressing, it thickens and becomes more horny; and one could multiply such instances almost indefinitely.

Secondly, there is a category of what may be called pseudo-exogenous adaptations, in which the animal exhibits characteristics similar to effects which can be called forth as direct exogenous adaptations, but which on investigation are shown to be hereditary, and independent of any particular environmental influence. We shall consider some examples of such adaptation in more detail later, since they pose one of the most striking problems to be solved.

Finally, there is a very large class of adaptations, which, as Medawar [1] has recently emphasized, need to be distinguished from the previous category, and which are characterized by the fact that the adaptive feature is of a kind which one cannot imagine as having ever been produced in direct response to the environmental conditions or mode of life of the animal. To give two examples only, Medawar mentions the modifications of certain epidermal cells to secrete sweat, and the development, from another part of the skin, of a transparent area which forms the cornea of the eye. It is, as he says, impossible to see how any attempt to peer through an area of opaque skin could tend to cause it to become

transparent. The adaptation of the cornea to vision can hardly have arisen in any causal dependence on external factors, and we might therefore give the name of endogenous adaptations to this category.

It is in connection with this third type of adaptation that we can as yet make the least progress beyond the current hypothesis, which is content to rely on the chance occurrence of suitable mutations. But even here there is a little more to be said. In some endogenous adaptations, the usefulness of the character is in connection with factors in the outside world. Another of Medawar's examples, the possession of horns which serve the purposes of aggression or defence, will suffice as an instance. But the transparency of the cornea is adaptive because it is suited to the functioning of another internal part of the organism, namely the retina, sensitive to the light which the cornea allows to enter. Now, I think that we shall often find that the various parts concerned in such internal endogenous adaptations are involved with one another not only during their functioning in the adult animal, but during their development in the embryo. This is certainly true of the cornea, which can be induced from normal epidermis if an eye-cup is transplanted under it at an early enough stage. All the various parts of the eye, which can function efficiently only if they have the correct relations with one another, are interdependent during their development. It was shown many years ago by Ross Harrison [2] that if the large lens of the axolotl *Amblystoma tigrinum* is grafted over the eye-cup of the smaller *A. punctatum*, the lens does not grow to its full size, while the eye-cup provided with the larger lens attains a greater size than usual (figure 1). Similarly, if the eye-cup of *A. tigrinum* is transplanted under the early embryonic skin of *A. punctatum*, it induces a lens which is originally of *A. punctatum* size and therefore relatively too small, but, as growth proceeds, the lens grows faster and the eye-cup more slowly than usual, so that they gradually achieve the normal relative proportions. We might say that the internal adaptation of the lens to its retina, although endogenous in the sense that it arises within the animal, is nevertheless affected by factors from outside the lens itself, namely by the retina. The problem it presents is therefore not wholly different from that offered by adaptations to external factors. Moreover, the adaptation is in part a direct response to the influence of the retina, and is thus similar to the first category distinguished above; but there is clearly also some inherent tendency for the *A. tigrinum* material to grow faster than the *A. punctatum*, and in this respect we are reminded of the second category, of pseudo-exogenous adaptations.

We may next consider the true exogenous adaptations, in which an animal becomes modified by external factors in such a way as to increase its efficiency in dealing with them. Such adaptation does not, of course, always occur: the environment may overcome the animal and eventually kill it. For instance, specialized breeds of cattle from a temperate zone growing up in the tropics may fail to become acclimatized, and, instead, develop into degenerate forms which have great difficulty in surviving. Even in such cases, however, there are probably always some tendencies towards the development of useful adaptations, though they are not strong enough to be effective. Adaptation to relatively slight changes in environment is, however, usually successful. We still know comparatively little as to how this is brought about, although we can speculate more or less plausibly about the mechanisms involved in particular cases. The hypertrophy of one organ of a pair when the other is removed (as in the case of kidneys) may, for instance, find its explanation in Haddow's suggestion [3] that each organ requires some special specific substance for its growth, or in Weiss's interesting work [4] on the effects on the growth of an organ of antisera specific against it (see also Ebert [5]).

It may be that, in many cases, the chemical processes involved in the functioning of an enzyme or

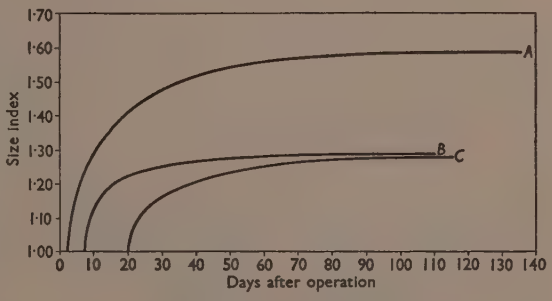


FIGURE 1 – *Transplantation of lens ectoderm from* Amblystoma tigrinum *to* A. punctatum. *Curve A: growth of the tigrinum lens when associated with the eye-cup of the same species, expressed as the ratio of the size of tigrinum lens to the size of punctatum lens. Curve B: similar curve for tigrinum lens associated with punctatum eye-cup. Curve C: growth of punctatum eye-cup associated with tigrinum lens, expressed in terms of its size when associated with punctatum lens. Note how in the interspecific combination the lens grows more slowly and the eye-cup faster than they would normally do (after Harrison).*

similar substance are related to those by which it is synthesized, so that increased function automatically means increased synthesis. Other examples are certainly more complex. For instance, if newt larvae are kept in water poor in oxygen, not only do the gills grow larger, but the tissue in their walls becomes thinner, allowing a more rapid diffusion of gas [6]. Possibly here we might be able to find some explanation in terms of the effect of oxygen-lack on the rate of blood-flow, and the influence of that in its turn on the vessels through which it is moving. But the phenomenon of adaptive response is so widespread and so general that it seems hardly convincing to explain it only by a series of *ad hoc* hypotheses, invoking a new one for each different case. At present, we hardly seem able to do better than go to the other extreme, and produce the general argument—too general to be very satisfying—that it is an advantage to animals to be able to adapt successfully to new circumstances, and therefore natural selection will have favoured those animals which by chance had a hereditary endowment which enabled them to do so. One feels that, somewhere between these extremes of particularity and inclusiveness, there should be principles of fairly general application to be discovered—but they still await their Darwin.

It is the remaining category of adaptations, the pseudo-exogenous, which has provoked the most discussion. We are confronted here by phenomena for which an explanation could so easily be found in a direct effect of some environmental factor, were it not that further study demonstrates unequivocally that the structure concerned is determined by the heredity of the organism, and is relatively independent of the environment. The question arises whether we can bring ourselves to believe that the part which the environment can play in mimicking the condition is really irrelevant, and that the evolution of this particular adaptation has resulted from the selection of chance mutations which might have appeared and produced the phenotypes even if the environmental effects had never existed.

Some concrete examples will make the problem clearer. One of the most familiar is that of the thickened skin on the soles of our feet. This thickening is obviously an adaptation to the stresses which this region of the body has to bear; but, as Darwin pointed out, and as Semon [7] discussed in a full-length paper, the thickening already appears in the embryo, before the foot has ever borne any weight. The structure therefore cannot be a direct response to external pressure, but must be produced by the hereditary constitution independently of the specific external influence to which it is an adaptation. The situation is even more striking when similar thickenings are found on less conventional parts of the body. For instance, the ostrich squats down in such a way that the under surface of the body comes into contact with the ground at its two ends, fore and aft. In just these places a considerable callosity develops in the skin (figure 2), and Duerden [8] showed that these thickenings make their appearance in the embryo before hatching. The same thing is true of callosities which appear on the wrists of the forelegs of the African wart-hog, which while feeding has a peculiar stance which involves resting on these points (Leche [9]). Another remarkably clear example, affecting a different organ, is that of the second molar tooth in the dugong. In the adult, the crown of this tooth is more or less flat, with slight transverse ridges. This shape must be regarded as a modification of an originally more conical tooth, and would at first sight appear to be directly related to the use of the tooth for grinding the food. However, Kükenthal [10] showed that, although the tooth first appears in a conical form in the early embryo, processes of resorption begin to change this into the final flattened form before the tooth is used (figure 3).

It certainly seems very far-fetched to attempt to explain such phenomena without bringing in the fact that the environment might be expected to produce similar effects. Let us consider, therefore, what might happen to an ostrich in which the appropriate callosities were not hereditarily determined. Presumably its skin, like that of most other animals, would react directly to external pressure and rubbing by becoming thicker. Now the point which seems to have been overlooked in previous discussions of the matter is that this capacity to react must itself be dependent on genes. Since populations of animals are never quite uniform in any character, we must expect that the ostrich ancestors varied in their capacity to produce the most suitable callosities; and there could be effective natural selection for those which performed the most satisfactory exogenous adaptation. A race would evolve in which the stresses set up by squatting in a particular way would call forth the development of appropriate adaptive thickenings of the skin.

At this stage, the thickenings would still not be hereditary and independent of the pressure and

FIGURE 2 – *The underside of an ostrich's body, showing the two callosities (redrawn from a photograph published by Duerden).*

rubbing; they would still be acquired characters in the conventional sense. We can find a hypothesis of how they might come to be hereditarily fixed if we turn to consider another aspect of the matter. The callosities are the results of developmental processes. Now, one of the main characteristics of animal development is that it tends to be canalized or buffered, so that the optimum end-result is produced even if there are minor variations from the normal conditions while the process is going on [11]. Natural selection, in fact, does not merely ensure that only those animals survive which have something near the optimum characteristics, but favours those genotypes which tend to produce such animals under any conditions. It gradually builds up efficient cybernetic mechanisms, to use a fashionable phrase. Thus we may expect to reach a stage in which our ostriches nearly always develop callosities of just the right size and position, even in those individuals which, to put it crudely, sit down very seldom or those which loll about the whole time.

Once such a cybernetic developmental mechanism has been built up, it will be rather like a gun set to go off when the trigger is pulled. The development of the callosities will proceed quite autonomously, once the process can be started. The initial stimulus, which may be a greater or lesser amount of external pressure, has become a relatively minor factor in the whole situation. It may then not be too difficult for a gene mutation to occur which will modify some other nearby region of the embryo in such a way that it takes over the function of the external pressure, interacting with the skin so as to 'pull the trigger' and set off the development of the callosities [12].

This may have seemed too long a train of argument to be very convincing, but a good deal of experimental evidence can now be produced to support it. In the first place, there seems to be no doubt that the formation of callosities on the sole of the foot is actually brought about by developmental interactions which go on in the embryonic limb-bud, as was suggested in the last paragraph. In animals which are hereditarily polydactylous, the genetic constitution causes an increase in the number not only of skeletal elements, but of the associated structures such as muscles, and, in particular, callosities (figure 4). These thickenings are therefore an integral part of the presumably complex but as yet unanalysed actions and reactions which mould the early limb-bud into the adult foot.

A more comprehensive check on the whole train of thought may be obtained if we imitate the postulated action of natural selection by artificially selecting for the ability to respond in some definite way to an environmental stimulus. No such work has been done on the formation of callosities, but an experiment has been made on

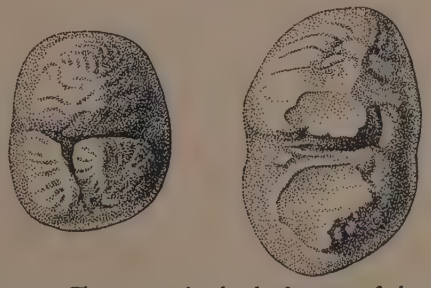


FIGURE 3 – *Two stages in the development of the second upper molar of the dugong. In the young embryonic stage on the left, the tooth has three conical protuberances, in which resorption is just beginning. In the older but still embryonic stage on the right, more or less flat faces have appeared (after Kükenthal).*

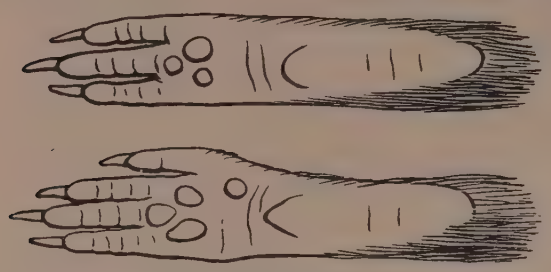


FIGURE 4 – *Right hind foot of a normal guinea-pig, above, and of a polydactylous guinea-pig, below (after S. Wright).*

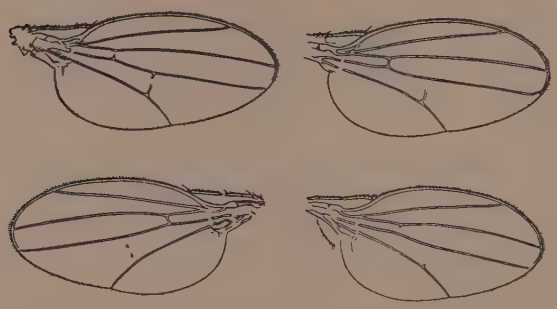


FIGURE 5 – *Defects of the posterior cross-vein in the wings of* Drosophila melanogaster *which had been given a temperature shock in early pupal life.*

the rapidly breeding fruit-fly *Drosophila melanogaster* [14, 15]. In order to make the situation as clear-cut as possible, an environmental stimulus was used which produced a phenotype which did not normally occur at all in the stock used. If pupae aged about 21–23 hours are subjected to a temperature of 40° C for four hours, a proportion of them develop wings in which the posterior cross-vein (and occasionally the anterior one) is broken or missing (figure 5). Two selection-lines were set up, in one of which only flies with broken cross-veins were used as parents; in the other, the flies which failed to react were selected. In both lines, the percentages of reactive individuals changed as time went on, increasing in the upward selected line and decreasing in the other. It is therefore actually possible to select for the capacity to respond to the environment (figure 6).

As the experiment proceeded, it confirmed further points in the theory given above. Stabilization of the type with broken or missing cross-veins did in fact take place, and proceeded so far that, as was predicted, strains could be produced which lacked the cross-vein even when they had been reared for their whole life under the standard normal conditions, and had never been subjected to the high-temperature treatment of their pupae. The cross-vein effect, which in the original stock had appeared only as a response to an external stimulus, is in these selected races quite independent of any special feature of the environment. We may say that the acquired character has been 'assimilated' by the genotype. Presumably, the lack of the vein is due now to some modification of the reactions which go on autonomously within the developing wing, but we do not know enough about the physiology of wing development in *Drosophila* to guess exactly what the reaction might be.

The gradual increase in the frequency of cross-veinless flies shows quite definitely that selection has been at work. It may, however, still be asked whether all that happened was the concentration of genic variants which were present in the population to begin with, or whether new mutations tending to break the cross-vein have arisen during the course of the selection, and, if so, whether we can suppose that the treatment has itself caused them to appear. The experiments which have been made so far do not allow of a final answer. It may be pointed out that the selected cross-veinless lines differ from the foundation stock in quite a large number of genes; we are not dealing with only a single gene, and if what we have collected are new mutations, there must have been a large number of them. Moreover, a considerable number of flies, of the order of a thousand, were involved in each generation, and it seems unlikely that new mutations could have been sorted out from such numbers in the comparatively few generations of the experiment. One cannot, however, absolutely rule out the possibility that the treatment provoked appropriate mutations. The main point is that there is no need to make this hypothesis, which is contrary to everything that we know about the mutation process.

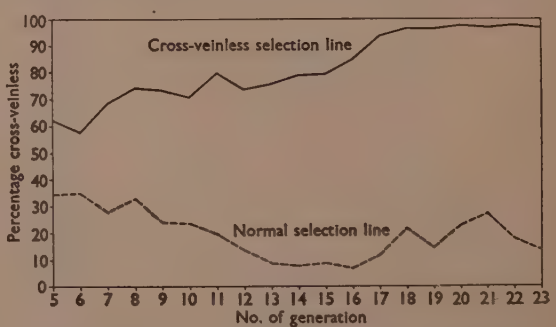


FIGURE 6 – *The results of selection for and against the ability to respond to a temperature shock by the formation of a cross-veinless phenotype.*

Selection of already existing genes which affect responsiveness to the environment, and stabilization of their effect, together provide a plausible account of the result in terms of orthodox genetic and embryological mechanisms.

It is probable that this process of genetic assimilation of an environmental effect has played a very important part in evolution. Pseudo-exogenous adaptations are very common in the animal, and also in the plant, world. Instances such as the ostrich's callosities and the dugong's tooth, which were discussed above, were chosen as particularly striking and impressive examples, not because they are typical; usually such adaptations have a much more ordinary character. One such case, which will also serve to illustrate some of the problems which remain to be cleared up, is that of the mountain forms of the common water snail *Lymnaea peregra* [16]. In certain tarns and loughs in Scotland and Ireland having very soft water, this snail occurs with an unusually thin shell, a form to which the name *L. praetenuis* has been applied. The thinness of the shell is clearly an effect of the lack of calcium in the water. It is found that when these forms are bred in water of normal hardness, they revert more or less completely to the normal; the effect in this case therefore is entirely, or at least mainly, an exogenous one which has not been genetically assimilated. But there is another method of economizing in shell-forming materials, which involves coiling the shell more nearly in one plane, so that the spire is reduced. Some lakes contain races which have adopted this shape, usually combined with a certain thinning of the shell; they have been given the varietal names *burnetti* and *involuta*. When they are bred in hard water, many of the races revert to normal, but in some of them the involute character is persistent, and must have been genetically assimilated. A whole series of questions suggest themselves. Why is the *praetenuis* form apparently never genetically fixed, while the *involuta* form sometimes is? Is it because the direct action of the environment is more effective in producing a thin shell of normal shape than a shell of altered configuration? Or is the thinness of the shell in *praetenuis* not truly an adaptation which is advantageous to the animal, but merely a necessary consequence of the lack of calcium, while the altered shell form of *involuta* has a selective advantage? And why has involution been genetically assimilated in some races but not in others? Possibly the length of time for which the lake has been colonized, or the degree of involution attained, may be important in this connection, but we still know too little to say.

It is clear that the theory of genetic assimilation may have wide applications, but before it can be used with confidence it requires much more experimental support than it yet has. The first thorough experiment made to test it gave the expected result, but that is hardly sufficient. Attempts are now being made with *Drosophila* to select for the capacity to give other responses to various environmental stimuli. In some cases, the experience with the cross-veinless character seems to be being repeated, but in others there has been little response to selection over the first few generations, and it may turn out that the original populations have little available variation in capacity to respond in the necessary way, in which case genetic assimilation would have no chance to operate. Until such limitations on the process have been more fully worked out, some caution is called for in applying the theory to all the phenomena for which it seems able to provide an explanation. However, it is at least not unimportant that we now have a hypothesis which gives a more or less plausible explanation of this large class of adaptations without invoking the discredited theory of the direct inheritance of acquired characters, and in a more convincing way than by a mere reliance on the occurrence of a suitable chance mutation.

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Biometry and the inductive method

KENNETH MATHER

Lord Kelvin said that 'when you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind: it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of science.' This is an extreme view, but it is undeniable that the evolution of an effective form of mathematical analysis has had, and is having, far-reaching consequences in biology.

While it would be foolish to deny the name of science to any branch of study merely because it makes but little use of measurement, no science can reach its flowering until it becomes quantitative in both its observation and its theory. Simple description and qualitative comparison can lay a groundwork, and can even lead to generalizations as basic as the cell theory in biology, but sooner or later the change from qualitative to quantitative becomes essential if progress is not to falter or even to halt. Not merely may generalizations lack full precision in the absence of a quantitative basis: they may even be impossible in the form that we know them. This is as true, for example, of Mendel's principles of heredity in biology as it is of Dalton's atomic theory in chemistry or Newton's laws of motion in physics.

Biology has been much slower in coming to its quantitative stage than have its sister, non-biological, sciences. In the last century, and even in the first decades of this one, it was virtually entirely descriptive and comparative in its content. Recent years, however, have seen a rapid change. Quantitative experimentation and, what is even more important, quantitative thought are now becoming commonplace. This move forward has been uneven and is still by no means complete, but it is in rapid progress and has already proved to be profound in its effects. Why has quantitative biology, biometry as we may call it, been so long in coming; and what has broken the deadlock and led to the advances of recent years?

In any experimental science we seek to proceed from the particular to the general. We make the basic assumption that, given corresponding circumstances, corresponding consequences will follow. Where the circumstances are exactly repeatable, so will be the results, and the particular observation then gives a firm basis for generalization. The less regularly repeatable the circumstances become, the more difficult it is to recognize their common element and the less sure our basis for generalization. Now an exact repetition of a situation may well in general be difficult or even impossible, but in the older sciences the variation can at least very often be reduced to insignificant proportions. A physical system or a chemical reaction can be reproduced sufficiently well for differences in the results of successive experiments, the experimental error, to be small as compared with the effect we are observing and measuring. Furthermore, the causes of great variation are usually sufficiently few and sufficiently clear for us to recognize them, measure their effects, and derive laws which enable us to make adequate allowance for them in our calculations. The volume of gas emitted by a system in chemical reaction will, for example, vary with temperature and pressure; but this brings little difficulty, for with the aid of Charles' and Boyle's laws we can make a satisfactory correction. In other words, the systems, or rather the variations of the systems, in chemistry and physics are sufficiently simple for us to pick out the agencies upon which they primarily depend, to measure the effects of these agencies, and so to make our observations repeatable within very narrow limits.

Biological systems are not simple in this sense. Organisms and their parts are highly variable for genetic, developmental, and environmental reasons, so that we can never reproduce a situation exactly. Furthermore, the agencies from which this variation springs are so many and so complex that we cannot be sure even of recognizing them all, still less of controlling them all. Nor can we in general pick out a few of them, control or measurement of which would so reduce the variation that the residuum would be insignificant. We must face a situation in which error-variation is ubiquitous, in large measure uncontrollable, and very far from negligible. So, in seeking to trace the effect of some treatment, change, or difference

in which we are interested, we are always confronted with the question of whether it is really a consequence of some other cause of variation which we may not have recognized or at least have not been able to control, and which is therefore confusing the issue. And in seeking to measure an effect we wonder how far this error-variation is vitiating our results. In other words, we must always be asking how far our information is reliable—for it is never fully repeatable—and hence how far we are justified in recognizing a specific common element in our varying situations.

In the past, biologists have sought to apply the method which has worked so well in chemistry and physics, that of seeking to recognize or introduce one or a few differences whose effects would be so great as to be unambiguously identifiable. This can work and has worked for gross effects, but as a method it is necessarily limited for two reasons. It denies us the ability to deal with the many agencies whose consequences, while important, may be no greater than those of the many others; and in any case the error-variation, though not great enough to prevent recognition of a gross effect, may still be sufficiently large to introduce a far from negligible uncertainty into the measurement of any relationship.

The classical approach to overcoming these difficulties is to seek ways of reducing the error-variation by standardizing both the organism and the environment in which it is reared and observed, so that the situation is made to approximate more closely to that with which the method can cope. Again there are two difficulties. In the first place, the task of describing and controlling the causes of error-variation is impossible. We can see many of the agencies which affect the fly in the culture-bottle or the plant in the field. We can reduce error-variation by controlling them. But we cannot yet render it negligible, for indeed there must be many agencies yet to be discovered. Must we wait until we have ascertained them all? Even then, would any experiment which required control of them all be humanly possible of execution, or, *a fortiori*, be justifiable by the standards of laboratory economics? And, let us not forget, it is still an assumption that we can standardize organisms and their development by external intervention. There may be events occurring inside cells which affect development and yet over which we cannot exercise any real control without ourselves drastically altering development. We may have the physicist's dilemma of uncertainty in a new and more immediately troublesome form.

The second difficulty is even more serious. Suppose we could do all this. Suppose we could produce our standard organism. How firm a basis would it give us for generalization? How far could the properties of one standard fly or one standard mould be taken as representing those of all flies or all moulds, even of the same species or race? To anyone familiar with biological systems, the hazard of assuming that any standard organism will satisfactorily represent the species or population will require little emphasis.

Thus, rather than seek to reduce error-variation to negligible proportions, we must accept it as a feature of biological systems, and try to devise means of conducting our experiments so that conclusions can be drawn despite its presence. We must learn to accommodate variation explicitly in our analysis, and to devise modes of thought appropriate to variable systems. To see how we must proceed, let us consider a simple question: how tall is a man?

At first sight there may seem to be no answer. Certainly there is no simple answer, in the way that there would be, for example, to the question of what is the boiling-point of water. Nor is there any simple correction which can be made by relating stature to some obvious component of the system so that variable observations could be corrected to a common level, in the way that pressure-changes can be accommodated in finding the boiling-point. Yet the question is not a meaningless one, for although we cannot answer it by a simple figure, we should have no doubt that objects 6 in or 12 ft tall are not men. Even figures of 3 ft on the one hand and 8 ft on the other would surprise us, although we might be prepared to admit that men can occasionally be of such statures. Clearly, although men may vary in stature, they do so over a limited range, and even within this range the more extreme statures are uncommon—or, to put it another way, less likely. The variation is thus something that can be described and codified. In short, we see that we must relate human stature not to a single figure but to a frequency-distribution telling us the proportions of men that fall within given ranges, or, conversely, telling us the chance that any man taken at random from the population will fall within a given range of stature. The frequency-distribution replaces the unique figure when we come to variable phenomena, and we proceed by estimating the parameters necessary to define the frequency-distribution. These are, of course, two, the mean and the standard deviation, in the case

of human stature, which has been found to follow the so-called normal distribution near enough for our purpose (figure 1).

Given the frequency-distribution, we can take the next step. Suppose we apply some treatment to one or more of our men—bring them up on a better diet or pick them out as being of some genetic type—and observe their stature. We know from the frequency-distribution the chance that this stature would have been found in men drawn at random from an untreated population, and we are then in a position to judge of the efficacy of the treatment by considering whether the observations would have been sufficiently unlikely, on the assumption of no effect of the treatment, for us to feel that in fact the treatment must have been effective. Our conclusion is not certain. There is always a chance that the apparent effect really springs from the normal variation in stature, but we at least know how likely this is. We can measure our uncertainty, and by doing so we are enabled to assess the significance of our observations, and to make rigorous statements about them and their causation.

The same applies where we seek to take a further step, and measure an effect which we have detected in the way just discussed. Any measure we reach will be made uncertain by the error-variation, but when we think in terms of frequency-distributions we can calculate and attach to our measure a statement of its uncertainty in the form of what is called a standard error. We may not be able to say that the dose of bactericide required to kill 90 per cent. of the bacteria is x; but we can say that there is a 95 per cent. chance that this dose lies between the limits $x - e_1$ and $x + e_1$, and a 99 per cent. chance of its lying between $x - e_2$ and $x + e_2$. Our answers are not simple, but they are rigorous and informative.

Therefore, when variation looms large in our observation, as it virtually always does in biology, our statements become statements of likelihood and our methods become statistical. Given the necessary statistics, however, we can be perfectly quantitative in our experiments, analysis, and thought. The reason why biometry languished until recently was because these necessary statistical notions and techniques were not available. The reason why it has moved forward so rapidly during the past few decades has been because these notions and techniques have become available at last. Yet the study of chances and probabilities is not a new discipline in mathematics: it goes back to Laplace, and beyond him into the earlier eighteenth century or even further. Why then was statistics of the kind the biometricians must use so long in coming? This question is worth a little discussion, for in answering it we can recognize another and most important feature of our present approach.

Statistical mathematics grew up from the discussion of games of chance, games played with apparatus which made their outcome uncertain. Various assumptions could, however, be made about this apparatus, such that even though the outcome of any one game remained uncertain, the possible outcomes could be listed and their frequencies in a large number of games calculated. We do not know what number a roll of the die will bring, but given that it is a 'true' die, we know that of a large number of rolls one-sixth

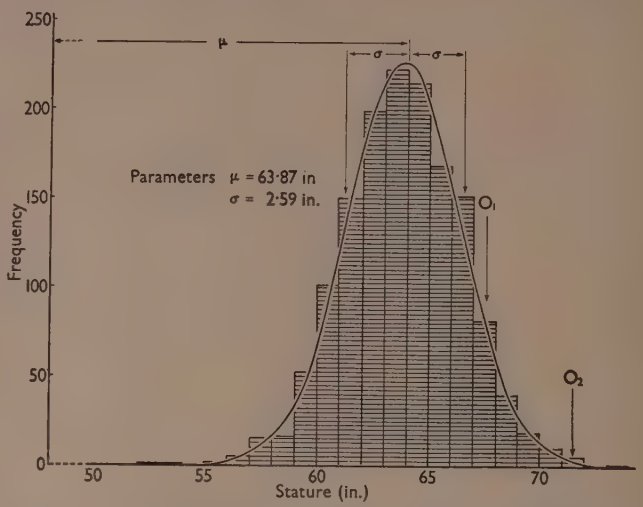

FIGURE 1 – *The frequency-distribution of stature in women. The histogram shows the frequencies (ordinate) of various statures, grouped in inches (abscissa), observed in 1456 women. The curve is the normal distribution representing stature in the population of which the women are regarded as forming a sample. The normal distribution is specified by two parameters: the mean, μ, which gives the average stature; and the standard deviation, σ, which, in being the distance from the mean of the points of maximum slope of the curve, measures the variation represented by the spread of the curve. The values given for the parameter are estimated from the observations. A stature of 67½ in (shown by O_1) is sufficiently common in the population which this distribution represents for no special significance to be attached to its observation in any single individual. A stature of 71½ in (shown by O_2) is, however, so rare and unlikely that its being shown by an individual following some treatment would normally be taken as constituting good evidence for the efficacy of that treatment.*

will yield a 1, one-sixth a 2, and so on. This type of statistics is deductive: given the properties of the apparatus, we deduce the statistical results. Deductive statistics has been, and indeed is still regularly, put to good use in science. The kinetic theory of gases, for example, requires a deductive statistical treatment; so also does genetics. But the deductive was not the type of statistics for lack of which the biologist was in difficulties. His problem was in fact the reverse. Given the observable consequences, he desired to reach conclusions about the system by inductive methods, and he very often desired to do so from the evidence which a necessarily small body of observations could yield. It was the statistics of inductive inference which the biological experimenter needed, and which became available to him only recently.

To Francis Galton in the late nineteenth century must go the honour of seeing the need to think constructively in this way about variable phenomena. He began that driving interest, the benefits of whose outcome we now enjoy. Then in 1908 'Student' (W. S. Gosset), himself a chemist, took the first step towards providing us with the means of reaching rigorous conclusions in the field of uncertain inference, when he calculated what is now called the *t* distribution, exactly relating observed quantities to their estimated standard errors. It was, however, left for Sir Ronald Fisher to develop and expound the principles on which rest the inductive statistics we now have. He gave us the logical basis, the mathematical structure, and the analytical methods. He taught us that our first task must be to secure a valid estimate of error-variation, in which can be included the effect of any agency, recognizable or unrecognizable, that we may wish; and he has shown us how we can reduce error-variation without vitiating its estimation. We have in fact a new branch of mathematical science, covering the design and analysis of experiments from the inductive point of view. The biologist seldom understands the mathematical basis of these methods, but he values them because he knows that they work, and he is using them more and more every year. And as he uses them, new problems of a mathematical nature are thrown up for the statistician's attention. It is a two-way traffic, and indeed quantitative biology must grow by the co-operation of biologist and statistician. Biometry without method is aimless, and statistics without use is sterile.

This new statistics has spread back from biometry into the older sciences wherever they meet variable phenomena. It has found wide application too in the field of engineering—for example, in quality-control—and has played its part through operational research in war. It arose first in relation to biology because biometry without inductive statistics was impossible; but having arisen it has gone on to prove its worth in the very sciences which could grow up without developing it. Once we explicitly recognized the principles upon which inductive conclusions must depend we had a more general method of approach capable of dealing with a wider variety of situations; more general because the older technique can be regarded as a special case in which the error-variation is capable of being reduced to the point where it is negligible, in the sense that the probabilities are sufficiently extreme for their calculation to be unnecessary.

The statistics of induction is a mathematics of experiment, and as such complements in its uses the deductive mathematics with whose principles we have been familiar, and upon which we have been building, since the time of Euclid. As Fisher pointed out in 1948, we have now begun to think constructively about variable phenomena, and to give edge and precision to the necessary thought-forms. The importance of these thought-forms extends beyond experimental research. They are essential for anyone who has to understand, guide, or manage any variable phenomenon, including human society. It may indeed be that our descendants will come to think of biometry as having begun to do for inductive reasoning what Greek geometry did for deduction two thousand years ago, and that they will regard instruction in the one to be as essential for a full education as we now regard instruction in the other.

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Ornithological illustration

W. B. ALEXANDER

The natural beauty of birds and their biological importance as one of the principal groups of the animal kingdom give an excellent opportunity for the simultaneous expression of scientific and artistic talent. The artistic merit of many of the older illustrated books is perhaps shown by the extraordinarily high prices they now fetch. Their value to the ornithologist lies in their exact portrayal of rare or extinct species, such as the dodo, of birds inhabiting inaccessible regions, and of characteristic postures in courtship and other activities.

Among the earliest artistic works of man, namely the Palaeolithic rock-paintings of southern France and Spain, pictures of birds are comparatively few. This is not surprising, since there can be little doubt that the primary object of the pictures was magical. Hence it was the large mammals, such as mammoth, rhinoceros, and bison, which were most often depicted on the walls of caves; large birds such as cranes, herons, and storks were, however, occasionally represented.

In a recently discovered cave at Lascaux, a remarkable scene shows a wounded bison pierced with a spear and, in front of it, the dead body of a man with his spear-thrower and ceremonial staff lying beside him. The man has a bird's head and his staff has a bird on its top, almost certainly showing that he was chief or high-priest of a bird totem, and that birds had magical associations as early as Palaeolithic times. Crude drawings of birds found in the Tajo Segura cavern in southern Spain are attributed to the Neolithic period; they depict birds which, when recognizable, are all of species still found in that region. They include the great bustard, raven, spoonbill, flamingo, and purple gallinule.

The first really artistic pictures of birds are found in frescoes in Egyptian tombs. According to R. E. Moreau, the earliest work is by far the best in both execution and accuracy; from Dynasty V (*c* 2500 B.C.) onwards the standard declines. 'At its best the Ancient Egyptian bird-portraiture is very good indeed; there was nothing in Western civilization to equal it until the nineteenth century A.D., 4500 years later.' Moreau considers that 45 species of birds are definitely identifiable. In the case of uncoloured reliefs, it is only species with very characteristic outlines that can be identified. When colouring came into fashion it was frequently inaccurate, either because only a few coloured pigments were available or because the colours of the bird were changed to harmonize with the general colour-scheme of the picture.

A fresco from Knossos in the Ashmolean Museum, Oxford, depicting Greek partridges and hoopoes, shows that Mycenean artists were little, if at all, inferior to those of ancient Egypt. During the classical period of Greece, however, little attempt seems to have been made to portray birds. In Roman times they were frequently depicted in mosaic pavements, but this was a medium unsuited to much accuracy of detail. The wall-paintings of villas at Pompeii show many brightly coloured pictures of birds.

During the medieval period, small pictures of birds were frequently used for the illumination of manuscripts, particularly those dealing with falconry. Some copies of the treatise on this subject by the Emperor Frederick II (1194–1250) have many marginal illustrations in colour depicting numerous species. Moreover, in medieval lore certain birds had legendary qualities or attributes which caused their introduction as accessories into religious paintings. Of these, the species most commonly depicted was the goldfinch, which appears, for instance, in Raphael's *Madonna del Cardellino*.

At a later period, wealthy Dutch burghers liked to keep strange birds, which were frequently painted by contemporary Dutch and Flemish artists. It is from such paintings that our knowledge of the aspect of the dodo, as it appeared in life, is derived.

The invention of the art of printing in the fifteenth century soon led to the preparation of woodcuts for the illustration of books on natural history. Two treatises on all known birds, each illustrated by woodcuts, appeared simultaneously in 1555; that of P. Belon in Paris, and that of K. Gesner at Zürich. In 1599–1603 there appeared in Bologna a similar, but even more comprehensive, work by U. Aldrovandi. The illustrations for these works differ much in

FIGURE 1 – *Great Horned Owl* (Bubo virginianus), *from Audubon's 'Birds of America,'* 1827–38. ($\times \frac{1}{4}$)

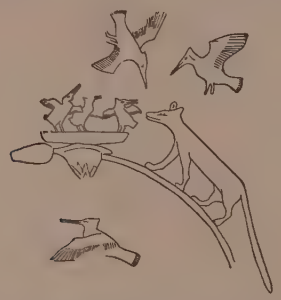


FIGURE 2 – *Pied Kingfishers* (Cergle mais), *attacking a genet-cat. From bas-relief in the tomb of Ti; Saqqara, Egypt.*

merit, but the majority of them are very crude.

At a much later period, woodcuts were used by Thomas Bewick to illustrate his 'History of British Birds,' but the fame of that work was due much less to the pictures of birds than to the remarkable little scenes introduced as vignettes. Woodcuts by A. Fussell formed the illustrations to the 'History of British Birds' by W. Yarrell, which was the standard work on the subject for many years, but in the writer's view the finest series of woodcuts of birds is that by J. Wolf, engraved by C. Whymper, which illustrated the earlier editions of 'British Birds in their Haunts' by C. A. Johns.

With few exceptions, the woodcut was soon superseded by the engraved copper-plate for illustrating serious works on ornithology. One of the earliest bird-books illustrated by plates was the *Uccelliera* of G. P. Olina, published in Rome in 1622.

During the seventeenth and eighteenth centuries it became fashionable to form natural history cabinets containing specimens from all parts of the world. As methods for preserving their skins were unsatisfactory, birds were generally represented by sets of paintings. To enrich such cabinets, naturalists travelled abroad, and some published illustrated accounts of their travels; in these works, birds commonly figured prominently. A noteworthy example is Mark Catesby's 'Natural History of Carolina, Florida and the Bahama Islands' (London, 1731–43), containing some of the earliest coloured pictures of North American birds. Another important work is François Levaillant's *Histoire naturelle des oiseaux d'Afrique* (Paris, 1796–1808), which contains coloured plates of many South African birds and some from other parts of the world. Earlier than this, Buffon had organized a scheme for publishing illustrations of animals, mostly birds, which aimed at depicting all known species. The plates were prepared by a team of over 80 French artists and assistants, and 1008 were published between 1765 and 1786. A supplement to these *Planches enluminées de Buffon*, containing illustrations of over 600 more species, was published by Temminck and Laugier de Chartreuse between 1820 and 1839.

It was, however, only the great libraries and the wealthiest patrons who could afford to subscribe for such comprehensive works. In consequence, most of the later folios with coloured plates dealt with the birds of a particular country or of a particular group or family. Of these, the families of birds with particularly brilliant plumage were the most frequently illustrated; examples are the parrots by Levaillant, from pictures by Barraband (1801–5), and by Edward Lear (1832).

Of books dealing with birds of specific countries, those on the birds of Britain have been the most numerous. The first set of plates of artistic merit was for the 'Illustrations of British Ornithology' by P. J. Selby (1821–34). The accompanying letterpress appeared in 1833. The large size of these plates allowed of life-size pictures of all but the largest birds.

In 1826, the French-American J. J. Audubon reached Edinburgh with his pictures of the birds of America, and Lizars, who had published Selby's illustrations, agreed to publish them. The very large double-elephant folio size of the plates, enabling the subjects of the pictures to be reproduced life-size, and the separate publication of the letterpress, followed the pattern already adopted for Selby's work. Owing to the difficulty of finding sufficient colourists in Edinburgh, Lizars had to discontinue the work for a few months, and the majority of the plates were eventually produced by Havill in London.

In his prospectus, Audubon claimed that the superiority of his drawings 'consists in the accuracy as to proportion and outline, and the variety and truth of the attitudes and positions of the figures. . . . The author has not contented himself, as others have done, with single profile views, but in very many instances has grouped his figures so as

FIGURE 3 – *Mallard* (Anas platyrhynchos), *from the tomb of Tehuti Hetep, Egypt.*

FIGURE 4 – *Ceylon jungle-fowl* (Gallus lafayetii), *from Des Murs'* 'Iconographie Ornithologique,' 1849. (× ½)

FIGURE 5 – *Tengmalm's owl* (Aegolius funereus), *from a painting by J. Wolf (dated* 1867) *in the possession of the author.* (× ½)

FIGURE 6 – *Brown or 'scarlet' ibis* (Guera rubia), *from Seligmann's version of the plate in Catesby's 'Natural History of Carolina, Florida, and The Bahama Islands,'* 1731–43. (× ½)

FIGURE 7 (*left*) – *Red and blue macaw* (Ara chloroptera), *from Lear's 'Illustrations of Parrots,'* 1832. ($\times \frac{3}{10}$)

FIGURE 8 (*right*) – *Red bird of paradise* (Uranornis ruber), *from Levaillant's 'Histoire des Oiseaux de Paradis,' Vol. I,* 1806. ($\times \frac{1}{3}$)

FIGURE 9 – *Mandarin duck* (Dendronessa galericulata), *from Gould's 'Birds of Asia,'* 1850–83. ($\times \frac{2}{7}$)

FIGURE 10 – *Head of bateleur eagle* (Terathopius ecaudatus), *from painting by Fuertes reproduced in 'Artist and Naturalist in Ethiopia,' by L. A. Fuertes and W. H. Osgood. (By kind permission of the Chicago Natural History Museum, and of Doubleday, Doran and Company.)* ($\times \frac{1}{2}$)

FIGURE 11 – *Great bustard* (Otis tarda), *from Selby's 'Illustrations of British Ornithology,'* 1821–34. ($\times \frac{1}{6}$)

FIGURE 12 – *Peacock* (Pavo cristatus), *from Belon's 'Nature des Oiseaux,'* 1555. ($\times \frac{2}{5}$)

FIGURE 13 – *Starling* (Sturnus vulgaris), *from Olina's 'Uccelliera,'* 1684. ($\times \frac{1}{2}$)

FIGURE 14 – *Woodcock* (Scolopax rusticola), *drawing by J. Wolf engraved by C. Whymper, from Johns' 'British Birds in their Haunts,'* 1899. (*Approximately original size.*)

to represent the originals at their natural avocations, and has placed them on branches of trees, decorated with foliage, blossoms, and fruits, or amidst plants of numerous species. Some are seen pursuing their prey through the air, searching for food amongst the leaves and herbage, sitting in their nests, or feeding their young; whilst others, of a different nature, swim, wade or glide in or over their allotted element.'

This seems to the writer to be a very fair description of the qualities of the great work which inaugurated a new era in the illustration of birds. The dramatic element in so many of his pictures appealed, and still appeals, to the public, but to the majority of ornithologists the poses often appear to represent positions which the birds could not maintain long enough to be visible to the human eye. They raise the question whether it is legitimate art to represent attitudes which could not be seen, in order to emphasize the vitality of the subject, or whether this is not rather a form of caricature. Audubon's plates of the birds of America were published in numbers from 1828 to 1838, and the text, entitled 'Ornithological Biography,' appeared in five volumes from 1831 to 1839.

While Audubon's work was still appearing, John Gould began the publication of a long series of folio works on birds, illustrated by coloured plates. The majority of the plates were drawn from skins, and depict birds with which the artist was not familiar in life, as in his monographs on toucans (1834), trogons (1838), American quail (1844–50), and humming-birds (1849–61), and in his books on the birds of the Himalayas (1832), of Asia (1850–83), and of New Guinea (1875–88). After starting a book on the birds of Australia, he decided to go to that country to study its birds at first hand, and he and his wife spent two years (1838–40) there. His book on the birds of Australia (1840–8) is undoubtedly the most important of his many works. Late in life he produced a book on the 'Birds of Great Britain' (1862–73), for which, however, he employed the assistance of other artists.

One of these was Joseph Wolf (1820–99), to whose drawings for woodcuts we have already alluded. Wolf was the eldest son of a farmer in Rhenish Prussia. In his early years, he devoted all his spare time to shooting and snaring birds and animals in order to have subjects to draw, and he realized that it was necessary to study their anatomy closely in order to make his drawings lifelike. At the age of 16, he persuaded his father to apprentice him to a lithographer in Coblenz; on completing his apprenticeship he returned home for a year and gave all his time to painting, in particular making a series of miniature bird-studies in water-colour. With these in his pocket he went to Frankfort-on-Main, and while there was advised to show his drawings to Dr Ruppell, who recognized their merit and invited

FIGURE 15 – *Ptarmigan* (Lagopus mutus), *from Millais' 'Game Birds and Shooting-Sketches,'* 1892. (× ½)

FIGURE 16 – *Jay* (Garrulus glandarius), *from a painting by B. Liljefors (dated* 1886). *(By kind permission of Mr N. E. Nilsson, Stockholm.)*

FIGURE 17 – *Bald eagle* (Haliaëtus leucocephalus), *from a painting by Allan Brooks. (By kind permission of Mrs M. Meiklejohn, Holt, Norfolk.)*

FIGURE 18 – *Brambling* (Fringilla montifringilla), *from a sketch by A. Thorburn in the possession of the Edward Grey Institute of Field Ornithology, Oxford.* ($\times \frac{3}{4}$)

him to draw illustrations for his forthcoming book '*Atlas zu der Reise im nordlicher Afrika.*' Thence he went to Darmstadt, and on Ruppell's recommendation showed his bird-paintings to Dr Kaup, the director of the museum. Kaup showed them to Professor Schlegel, with the result that Wolf was invited to draw illustrations for the great *Traité de Fauconnerie* by Schlegel and Wulverhorst, published from 1844 to 1853. From this time onwards, he obtained plenty of employment in painting and lithographing birds, especially birds of prey, for various works. In 1847 he went to Antwerp, but in the following year decided to accept an invitation to London, which he had previously refused. There he soon became recognized as the leading animal painter of the day, and obtained ample work as an illustrator of scientific papers in zoological and ornithological journals and books. In the writer's opinion he far surpassed all previous bird-painters, and has remained unequalled in his capacity to make birds appear alive.

More recent bird artists (excluding those still living) whose work approached or equalled the standard set by Wolf include Archibald Thorburn, J. G. Millais, Louis Agassiz Fuertes, Allan Brooks, and Bruno Liljefors.

Archibald Thorburn (1860–1935) was the fifth son of Robert Thorburn, the foremost miniature painter of his time. He began by painting flowers, and in many of his bird pictures the beauty and delicacy of the surrounding flowers reveal the accuracy in detail of the miniaturist. His first important engagement was to complete the plates in Lord Lilford's 'Coloured Figures of the Birds of the British Isles' when J. G. Keulemans could not continue through ill-health. Thorburn frequently visited Lilford Hall, where the aviaries contained many of the birds portrayed, and it is known from correspondence that he must have benefited greatly from the advice of his patron. Perhaps the chief criticism that can be made of his work is that he almost always depicted his birds in perfect plumage and in their brightest colours; thus they often appear too brilliant.

John Guille Millais (1865–1931) was the fourth son of Sir John Millais, a president of the Royal Academy, and was from boyhood an ardent sportsman and naturalist. He hunted and fished in many foreign countries, and illustrated the many books he wrote with spirited drawings and sketches of scenery and animal life. His chief works on birds were on the game-birds and the ducks of the British Isles, and he was specially interested in the various plumages and moults of

FIGURE 19 – *Great crested grebe* (Podiceps cristatus), *from Gesner's 'Historiae Animalium liber III, de Avibus,'* 1607. (× ⅛)

these birds and in their behaviour. In his 'Natural History of British Game Birds' the main coloured plates are from pictures by Thorburn, but the author himself depicted their display and other activities. In the opinion of the writer these drawings of Millais are little, if at all, inferior to Thorburn's artistically; they are certainly more spirited. It is a loss to science that Millais died before the completion of his projected work on the display of birds.

Louis Agassiz Fuertes (1874–1927) was born at Ithaca in the United States. He began drawing birds without suggestion or guidance from others, and for thirty years his activity and industry were amazing. Of the books for which he painted long series of illustrations, perhaps the most important were Eaton's 'Birds of New York' (1910) and Forbush's 'Birds of Massachusetts' (1925–9), but he was constantly in demand to illustrate magazine articles, pamphlets, reports, and scientific papers. In the words of one of his biographers: 'Other artists and good ones came into the field, but it was Fuertes who set the standard, who inspired the ideal of all, and by abundant production spread broadcast the charm and beauty of birds, not merely in accuracy of line and colour, but in the expression of subtle intangible qualities approaching spirituality.' His capacity for producing new illustrations of species which he had already depicted many times was undoubtedly due to his own intense enthusiasm for his subject and his constant study of birds in the field. His knowledge of birds of the western hemisphere was almost unrivalled. He joined expeditions to Alaska, Canada, Mexico, and South America, and finally to Abyssinia, and he visited most parts of the United States. Perhaps the finest examples of his work were paintings made on his Abyssinian expedition, published, after his death, in 'Abyssinian Birds and Mammals' (1930) and in 'Artist and Naturalist in Ethiopia' (1936).

Allan Brooks (1869–1946) was born at Etawah, India, but in 1895 settled permanently in British Columbia. At first he made a living by collecting mammals, birds, and eggs for museums and dealers, and by trapping fur-bearing mammals in winter, but from about 1904 he became known as an artist, and about 1906 began painting illustrations for Dawson and Bowles' 'Birds of Washington,' published in 1909.

It does not appear that Allan Brooks had any formal artistic training. He was primarily a naturalist, and regarded himself as an illustrator whose prime object was accuracy in every detail. Thus he constantly travelled to different parts of Canada and the United States to become familiar with the habitats of the various species he depicted, and to collect specimens in all stages of plumage. Among his more important works were the paintings for Dawson's 'Birds of California' (1923), which he had begun before the 1914–18 war, a complete series of all the birds of North America accompanying articles published in the *National Geographic Magazine* from 1934 onwards, and the completion of the plates for Forbush's 'Birds of Massachusetts' after the death of his friend L. A. Fuertes.

Bruno Liljefors, born in Sweden about 1860, lived an open-air life and was intensely interested in nature from his earliest youth. As a young man he was an ardent sportsman, but in later life was content to watch animals and birds without pursuing them. After a few years of study, including a few months under the instruction of the animal painter Deyker, of Düsseldorf, he married and settled in a country home near Uppsala. His earlier pictures are mostly of creatures in the forest and show elaborate detail. When a little over thirty he moved into the Stockholm archipelago and in these new surroundings painted many pictures of seabirds in flight in a much more impressionistic style. In almost all his pictures the background is important, as indicating the habitat of the creatures portrayed, and the animals or birds are shown in action.

Progress in metallurgical microscopy

B. W. MOTT

The development of new techniques, and improvements in already existing methods, of examining opaque specimens with the optical microscope have resulted in considerable progress in the determination of the surface structure of metals. In particular, contrast has been increased by the incorporation in the apparatus of suitable stops and phase-plates, and useful results have been obtained by the use of polarized light and interference methods.

In optical microscopy, the introduction of new techniques, and recent developments in old ones, have resulted in a wealth of new information for the metallurgist. These advances have been supported by the advent of electron microscopy and of hardness-testing at low loads, and by improvements in the methods used for the preparation of metallographic sections. The present article describes some of the more important modifications in the metallurgical microscope which have been developed in recent years, and indicates the usefulness of the new techniques.

The basic design of the metallurgical microscope has remained relatively unchanged, and the type of illuminating train which gives the best results is that described by Greaves and Wrighton [1], shown diagrammatically in figure 1. The positions of the components should be adjustable to enable the condition of critical illumination to be obtained. This setting ensures that the illuminating cone is such as to use the full aperture of the objective, and at the same time prevents the introduction of stray light, which would take no part in the formation of the image. The plain glass slip formerly used as a vertical reflector has been improved by coating the lower surface with zinc sulphide, to increase the reflectivity, and the upper surface with magnesium fluoride, to suppress double-image formation.

The efficiency of the coated-glass reflector, in terms of the relative intensities of incident and transmitted light, is from 20 to 25 per cent., compared with about 5 per cent. for a simple glass slip unit. A further increase in efficiency, to 45–50 per cent., can be obtained by using the Foster calcite prism reflector [2] which has been fitted to the Bausch and Lomb metallograph. Another fitting on most modern metallurgical microscopes is a rotating stage; this is essential for work with polarized light and is useful for other methods of examination.

TECHNIQUES FOR INVESTIGATING SURFACE TOPOGRAPHY

Contrast and detail can often be improved by stopping-down the iris of the lamp, but the quality of the image is then impaired. By making use of the phase-contrast principles developed by Zernicke [3], the phase-difference in the reflected light from two areas of a specimen differing in surface level by about 200–500 A can be converted into differences of intensity in the image. This may be achieved by using a hollow cone of light, produced from an annular aperture placed immediately behind the iris, and by incorporating a phase-plate of a suitable size between the vertical reflector and the eyepiece. The phase-plate has an annulus for advancing or retarding the light which it transmits by a quarter of a wavelength relative to that transmitted by the rest of the plate, giving positive or negative phase-contrast respectively.

The chief use of phase-contrast in metallography is to improve the distinction between two phases which under normal illumination may be only just differentiated by stopping-down; the apparatus

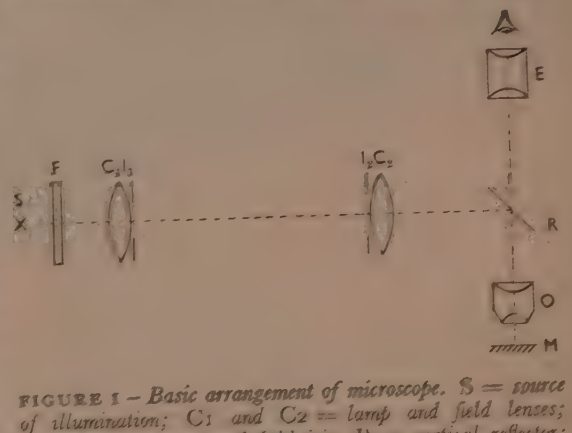
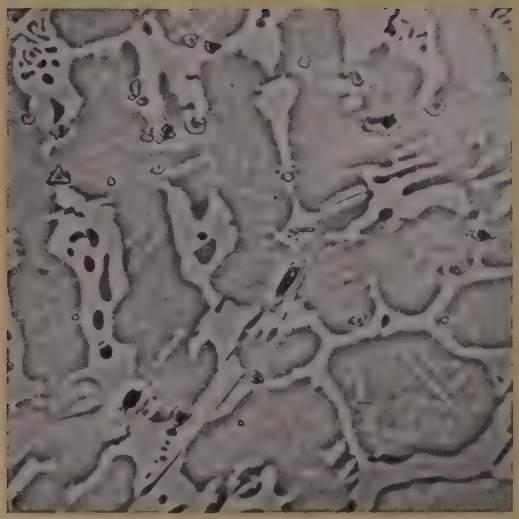


FIGURE 1 – *Basic arrangement of microscope.* S = *source of illumination;* C_1 *and* C_2 = *lamp and field lenses;* I_1 *and* I_2 = *lamp and field iris;* R = *vertical reflector;* O *and* E = *objective and eyepiece lenses;* M = *specimen;* F = *monochromatic light filter.*

FIGURE 2 – *Rotation of electropolished bismuth under crossed polarizers with a sensitive tint-plate inserted.*

and results achieved have been described by various authors [4–6]. An example of the increased contrast obtainable is illustrated in figures 3(*a*) and 3(*b*), which show a specimen of nickel-bearing cast-iron with and without phase-contrast respectively. Another application of the technique is in studying the topography of a surface; this can be determined without ambiguity, provided that the differences in surface-level are within the range mentioned above. For example, the relative rates of attack of two phases on etching may be ascertained by observing which appears the lighter under phase-contrast examination. The method may be extended to a determination of whether small areas observed under ordinary illumination on an etched surface are in fact pits or a lightly attached precipitate on the surface.

The use of dark background and oblique illumination for revealing irregularities in a surface is well known, but the sensitivity of these methods is seriously limited by the numerical aperture of the objective. A recent development due to Lomer and Pratt [7], which is described as the opaque-stop technique, may be used to detect surface-slopes with a much greater sensitivity, equal to about 1′ at a magnification of × 6, and 1° at



(a)

(b)

FIGURE 3 (*above*) – *The principal value of phase-contrast microscopy is in increasing contrast. These two photomicrographs are of a specimen of nickel-bearing cast iron,* (a) *with phase-contrast,* (b) *with ordinary illumination.* (× 250)

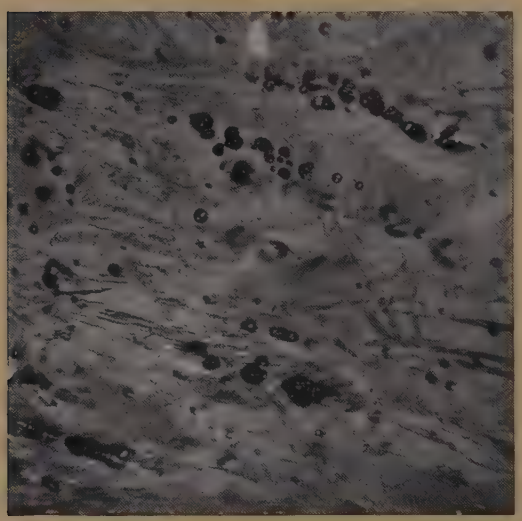
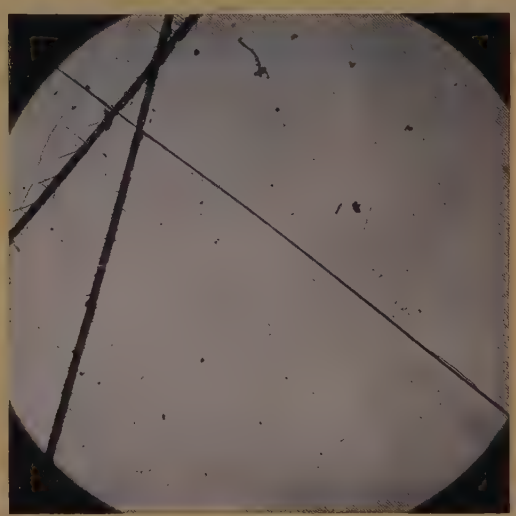


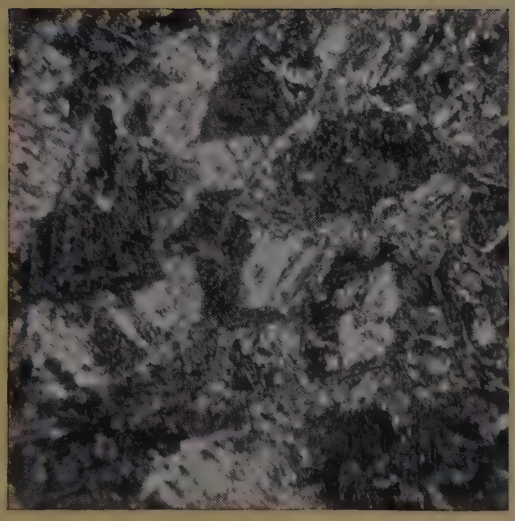
FIGURE 4 (*left*) – *Preferred orientation in cold-rolled uranium. Polarized light.* (× 125)

FIGURE 5 (*below*) – *Deformation structure associated with twinning in zinc,* (a) *with opaque stop,* (b) *with ordinary illumination.* (× 30)

(a)



(b)



(a)

(b)

FIGURE 6 (*above*) – *Determination of austenitic grain-size in a martensitic steel,* (a) *with polarized light,* (b) *with ordinary illumination.* (× 200)

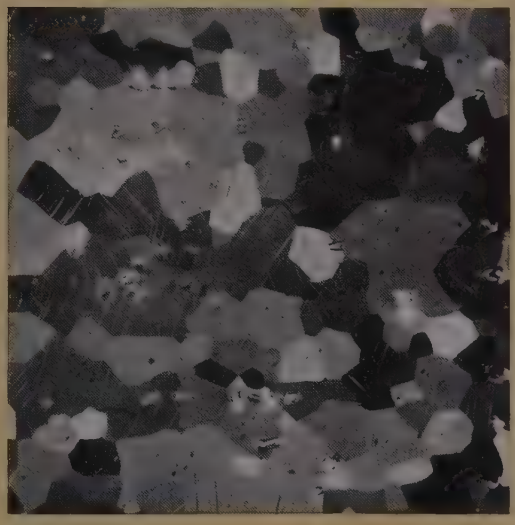
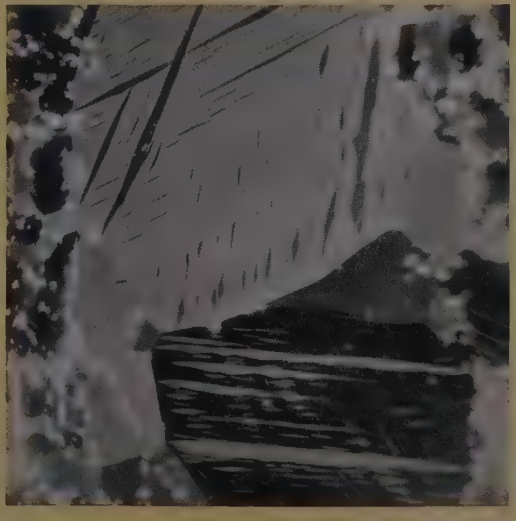
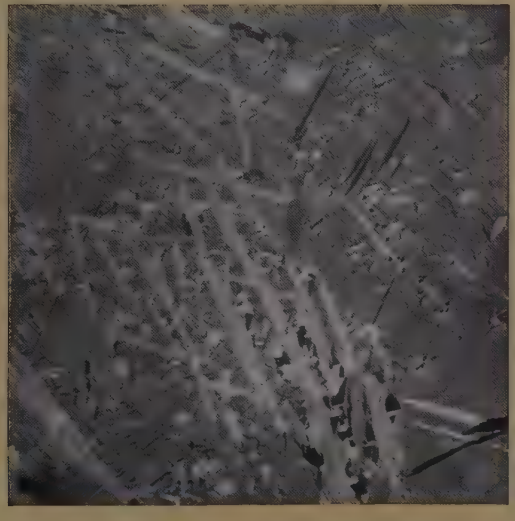


FIGURE 7 (*right*) – *Recrystallized uranium bar. Polarized light.* (× 250)

FIGURE 8 (*below, left*) – *Fine twinning in hot-pressed beryllium powder. Under polarized light.* (× 250)

FIGURE 9 (*below, right*) – *Alpha-uranium separating from the beta-phase in a U-Cr alloy. Polarized light.* (× 250)





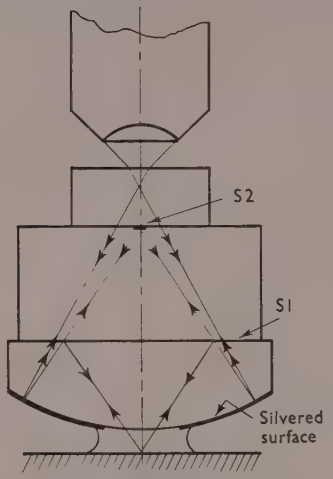


FIGURE 10 – *Dyson interferometer microscope.* S1 = *half-silvered surface;* S2 = *silvered spot.*

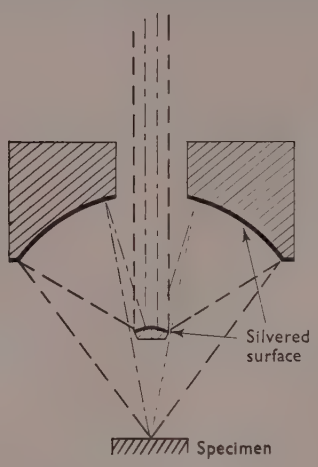


FIGURE 11 – *Beck reflecting objective.*

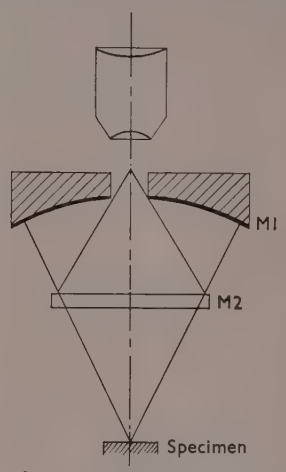


FIGURE 12 – *Dyson long working-distance attachment.* M1 = *spherical mirror;* M2 = *half-silvered mirror.*

× 200. The principle of the method is to cut out the undeviated rays from the specimen, and to form an image with the diffracted rays only. For high powers, this is best achieved by the use of an annular aperture, as in phase-contrast work, combined with an annular stop of appropriate size placed between the vertical reflector and the eyepiece. Alternatively, a straight-edge stop may be used in conjunction with a point-source; inclinations can be determined from the distance the stop must be traversed to eliminate the light from each inclined face of the specimen. The technique is extremely useful for studying mechanisms of deformation by the examination of cleavage-faces, etc., and some results for zinc have been described by Pratt and Pugh [8]; two of their photographs are given in figures 5(*a*) and 5(*b*). The complexity of the movements which accompany twinning in zinc is shown in figure 5(*a*) by use of the opaque-stop technique; the movements are not, however, revealed in figure 5(*b*), which is of the same area under ordinary illumination.

Variations in level of as little as about 25 A may be detected by the multiple-beam interference technique developed by Tolansky [9], in which interference-fringes are produced by a wedge-shaped air-gap between a silvered, optically flat glass plate and the specimen. Any displacement of the fringes in the image is related to a difference in level on the specimen. Although theoretically the incident beam should be parallel, useful results can be obtained with low-power objectives without making any special provision of this kind. As an example of the application of the technique, Tolansky [10] studied the surface-distortions of metallic surfaces in the region of indentations made with diamond, and was able to relate the interference patterns observed to the nature of the properties of recovery of various materials. Two different types of pattern occur; thus the pattern is symmetrical round an impression in isotropic steel and asymmetrical in anisotropic tin. Tolansky has recently described simple modifications of his original technique, involving the use of films of Canada balsam on the specimen, permitting studies to be made at high magnifications [11].

Dyson [12] has designed an apparatus, illustrated in figure 10, which is interposed between the objective and the specimen, and will resolve differences in level of about 30 A. The light initially transmitted by the objective is divided at a half-silvered surface, S1, such that part is focused on a silver spot, S2, and part on the specimen. Interference occurs between the two resulting beams, which have been subjected to a difference in optical path, and this can be controlled by an axial movement of the glass plates. A small magnification results from the system, so that the numerical aperture of the objective is effectively increased.

THE USE OF POLARIZED LIGHT

The theory of reflection of plane-polarized light from anisotropic surfaces was first considered by Jamin in 1847 [13], and was further developed by Drude in 1887 [14]. It is only in recent years that extensive use has been made of polarized light in metallography, and the increased interest in its

application has resulted in several publications which should be consulted for detailed accounts of the technique [15, 16]. The additional apparatus required for visual work is simple; it consists of a polarizer unit placed immediately in front of the vertical reflector, and an analyser unit between the reflector and the eye. Good-quality polarizing-sheet is preferred to Nicol prisms, as there is no limit to the aperture for full polarizing efficiency. The objective lens should be free of strain, since strain may result in anomalies from the superimposition of birefringent effects on the polarization state after reflection by the specimen [17]. The type of coated-glass reflector described above gives a more uniform polarization over the field of view than is given by a plain slip, and the intensity of the light is appreciably improved. Alternatively, the Foster prism [2] may be employed, since it serves as a polarizer, vertical reflector, and analyser. With this unit, the equivalent of rotation of the analyser from the crossed position cannot be obtained directly, although an approach to it can be produced by placing a quarter-wave plate between the objective and the reflector, which induces slight ellipticity in the incident beam.

In the crossed-polarizer condition, and in the absence of stray polarization effects in the apparatus, a complete rotation of an anisotropic single crystal will give four maxima of equal intensity. The positions of the maxima and minima of intensity will depend on the orientation of the reflecting surface, so that, for a given setting of the microscope-stage, the grains in a multigrained specimen may be identified by differences in intensity. By rotation of the stage, differences in orientation can be observed, and areas differently orientated by as little as 2° may be distinguished. If the ellipticity of the reflected beam is sufficiently low, the grain-contrast may be improved by slight rotation of the analyser from the crossed position; this also reduces the number of intensity-maxima from four to two per stage rotation [18]. All anisotropic metals and alloys can be studied under polarized light if prepared so as to avoid surface-flow and other imperfections [19], but cubic metals must be etched to give elliptically polarized reflected beams resulting either from a birefringent surface film which shows epitaxy (oriented overgrowth), or from a regular array of pits in which multiple reflection occurs at oblique incidence [15].

Since the stage-setting for minimum intensity varies with the orientation of the grain, it is possible to obtain an estimate of the degree of preferred orientation in a metal from the fraction of the area of a section having approximately the same extinction angle when viewed under crossed polarizers. Figure 4 shows areas of preferred orientation in a cold-rolled uranium bar cut in longitudinal section. Dunsmuir [20] has described a method of checking the preferred orientation in sheets of an iron-silicon alloy used for magnetic purposes; it is based on examination in polarized light after the development of pits by etching. A quantitative development of this method was used successfully by Woodard [21], who made photometric measurements of the changes in intensity in the reflected light as specimens of Monel metal were rotated. He showed that with increasing deformation the four intensity-maxima became more pronounced, owing to an increase in preferred orientation, but that fully recrystallized metal behaved as randomly orientated material.

A visual test for preferred orientation, applicable to etched metals, in which the reflected light has marked ellipticity, is made by inserting a sensitive tint-plate between the vertical illuminator and the analyser. Under these conditions, a difference in ellipticity is revealed by a difference in colour, and, since the ellipticity varies with the azimuth of the plane of polarization, the colour of a given grain will undergo a regular sequence of changes on rotating the stage. Two grains will show the same simultaneous sequence of colour-changes only if they have identical orientations. Figure 2(*a*)–(*d*) shows colour-changes in an electrolytically polished specimen of bismuth when rotated under these conditions; it will be seen that, although for some stage-settings the colour of the twins merges into that of the parent grain, they are clearly distinguishable on further rotation. The plane of the central violet grain, which remains the same colour throughout rotation, must be perpendicular to the optical axis, i.e. the main trigonal axis, and this is confirmed by the general threefold symmetry of its outline.

One of the outstanding features of the examination of metals under polarized light is that the surfaces may often be viewed while still in the condition as polished; hence it is possible to study fine details which are liable to be destroyed by the etching necessary for examination by more conventional techniques. Thus, recrystallization and deformation characteristics can be investigated, and the technique is especially useful for metals such as uranium [22], beryllium [23], and zirconium [24, 25], where difficulty is experienced in

revealing small differences of orientation by conventional etching-methods. As examples of the results that can be obtained, figure 7 shows the structure of recrystallized uranium, in which groups of closely orientated grains are present; figure 8 illustrates the fine twinning detail in a specimen of hot-pressed beryllium powder.

An anodic treatment, originally described by Hone and Pearson [26] for examining aluminium is often used to investigate the structures developed after the metal has been subjected to deformation and recrystallization [27–29]. Mott and Haines [19] have used polarized light for measuring the austenitic grain-size in a martensitic steel, since this is not easily identified on etched sections under ordinary illumination. The improvement in grain-contrast is clearly shown in figures 6(*a*) and 6(*b*), which were taken with and without polarized light respectively.

In a multiphased alloy, it is often difficult to distinguish the phases by etching if they are of similar compositions. Under crossed polarizers, however, it is easy to differentiate between a cubic phase, which remains extinguished on stage-rotation, and an anisotropic phase, which shows a variation in intensity [19]. In the case of two anisotropic phases occurring together, some distinction may also be obtained if the degree of optical anisotropy is sufficiently different. This is illustrated in figure 9, which shows a specimen of uranium-chromium alloy containing both alpha- and beta-uranium solid solutions [30]. The markedly anisotropic alpha-separations are easily distinguished from the beta-matrix of lower anisotropy. A special case of phase-identification is that of non-metallic inclusions in steels and non-ferrous alloys; by using polarized light, information may be obtained of the shape, transmission colour, crystal symmetry, and pleochroic characteristics [31–33].

MICROSCOPY OF HOT METAL SURFACES

Examination of metal specimens at room temperature reveals details of the structure which is stable at such temperature, or which has been retained on cooling from a higher temperature. It is very often advantageous to examine changes in structure, such as recrystallization, grain-growth, or phase-transformations as they occur at high temperatures. Apparatus suitable for this purpose has been described by various authors [34–37]; it usually consists of a chamber, for containing the specimen in a high vacuum or in an inert atmosphere to reduce oxidation, fitted with an optically-worked silica window through which the specimen may be observed. Adequate cooling of the walls of the chamber must be provided in order to protect the objective, the working distance of which must be sufficient to clear the silica window. For this work, it is advantageous to use a reflecting objective of the type described by Burch [38], which has a numerical aperture of 0·65, comparable with that of a 4 mm refracting objective, and a working distance of 14 mm. A modification of the Burch objective which uses two spherical mirrors (figure 11) has been put on the market. Alternatively, an attachment designed by Dyson [39] may be employed to increase the working distance of a 4 mm objective to about 13 mm. Figure 12 shows the design of the attachment, which consists of a spherical mirror M_1 such that the object is at its centre of curvature, and a half-silvered plane mirror M_2, placed midway between M_1 and the specimen, which reflects the image into the focal plane of the objective.

Studies which have been carried out at high temperatures include those of Forsythe [40] on the effect of fatigue on the structure of various metals, of Maréchal and Doucet [37] on the recrystallization of copper, of Olney [35] on the formation of graphite on the surface of hypereutectoid steels on heating, and of Brinson and Moore [41] on the recrystallization of zinc; the last was observed under polarized light.

CONCLUSION

Many new techniques have recently become available to the metallographer, who is now in a position to examine structures in far greater detail than ever before. For example, in a study of the topography of a surface, both the interference and the opaque-stop microscopes may be used to provide confirmation of observations made under phase-contrast illumination, and for quantitative measurements. To obtain the maximum usefulness from the microscope, the metallurgist must examine his specimens by more than one method. A judicious combination of the techniques described in this article can lead to a clearer understanding of the important physical processes involved in the thermal and mechanical treatments of metals.

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Book reviews

PROTEIN SYNTHESIS

La synthèse protéique, *by E. F. Terroine. Pp.* 539. *Centre National de la Recherche Scientifique, Paris.* 1952. *Fcs.* 3200 *net.*

The elucidation of the mechanism of protein synthesis is undoubtedly one of the most important problems in biology. The author points out that, in spite of the considerable amount of work which has already accumulated (he cites 1809 references), the information at present available on this form of biosynthesis is very sketchy, and often contradictory. However, as the author pertinently remarks, despite the importance of the subject 'man prefers to talk nonsense rather than to keep quiet.' Nevertheless Professor Terroine himself does not stray from the paths of reason and, though he may have no illusions about the tentative character of the mechanism of synthesis he suggests, the assumptions he puts forward to support it are all based on established facts. For many years he has been studying the metabolism of nitrogen: his book is a summary.

It is composed of two parts. The first, of 175 pages, deals with the formation of the basic materials of protein synthesis, namely the amino acids; proofs of the genesis of certain of these; details of the synthetic limitations of organisms; and mechanisms of synthesis. The second part, of 274 pages, deals with the combination of amino acids, that is to say with protein anabolism proper; the constitution of proteins; their characteristics; conditions, sites, and mechanisms of synthesis; and determining agents.

This is a valuable account of a difficult topic; however, judging by the number of question-marks scattered about the text, the solution of many problems must still be left to the sagacity of the reader. R. DELABY

TIMBER TROUBLES

Dry Rot and other Timber Troubles, *by W. P. K. Findlay. Pp.* 267, *with half-tone illustrations. Hutchinson's Scientific and Technical Publications, London.* 1953. 25*s. net.*

Dr Findlay's book ranges further than its title indicates. We expect from him, and receive, an authoritative account of all the activities of the dry-rot fungus: we are given, in addition, comprehensive descriptions of the fungus diseases of standing trees, and of the destruction of wood by insects. The section on insect damage brings together for the first time a record of the advances in this field made by Findlay's

colleagues at the Forest Products Research Laboratory. Other chapters deal with the physical and chemical composition of wood, with causes of deterioration, and with discolorations, stains, and blemishes of timber.

It is in the chapters dealing with measures of control that the book reveals its distinctive character, which arises from the author's ability to be at home in two worlds: that of the mycologist and that of the user of timber. Findlay's evident sympathy with, and understanding of, the problems of the timber merchant, the architect, the boat-builder, and the gardener gives his recommendations the authentic ring of practicability. His chapters on care of timber, on wood preservation, and on the prevention of decay reveal the alarming waste of our timber resources. They emphasize the fact that much of the destruction is preventable, and make clear the means by which it could be ended. R. W. MARSH

CHEMISTRY FOR EVERYMAN

General and Inorganic Chemistry, *by Alexander Findlay. Pp. x + 239. Methuen and Company Limited, London.* 1953. 8*s.* 6*d. net.*

It is important, in a period of history when science is markedly influencing the social order, that there should be available for the laymen books such as the one under review. The 'Home Study Books' have been planned to enable authorities to write briefly and simply, yet without facile popularization, upon the subjects of which they are masters. In this new volume, Alexander Findlay describes with expert knowledge and acumen the more important chemical phenomena met with in everyday life, and outlines the great advances in our knowledge of the nature of matter and the structure of the atom. He also deals with the more familiar elements and their compounds, but, while including carbon as the best known of the elements, does not discuss in detail matters appropriate to organic chemistry. The form and content of this book meet the needs of young people intending to follow a scientific career, and should also appeal to the intellectual interests of that wider public who wish to gain some knowledge and understanding of the science of chemistry. Actually this is one of those rare books which the expert can enjoy yet which cannot fail to be profitable for the beginner. Printing and binding are excellent. The author and the publisher deserve congratulations on a notable achievement. W. WARDLAW

ORGANIC AND ARTIFICIAL MANURES

Manures and Fertilizers, *by A. M. Smith. Pp. 275. Thomas Nelson and Sons, Edinburgh.* 1952. 15*s. net.*

In the drive for increased food production it is important that the grower should have access to the latest information and basic principles of a subject that plays so important a part in the growth of crops. This book is therefore a welcome and very valuable addition to the series of Nelson's books on agriculture.

Dr Smith is an expert on manures and fertilizers, and the value of his long experience in advisory work, research, and lecturing is shown in the clear and balanced presentation of both theory and practice. There has been careful pruning to eliminate non-essential matter. Much against his wish, the author has retained the use of the symbols P_2O_5 and K_2O; many will agree with him that these nutrients would be much better expressed as the elements phosphorus and potassium, for this would at least bring them into line with nitrogen.

The book opens with chapters on the nutrition of the plant and the nature of soil organic matter, and these form a useful and logical lead into the discussion of organic manures and fertilizers. Adequate treatment is given of the various types, sources, and production of these materials. Their functions in relation to plant and soil are clearly defined, and the facts as set out in this book should clarify any confused ideas that still exist about 'organics' and 'artificials.' In the sections dealing with the chemistry of the manufacture of fertilizers, the author has included the most up-to-date information: in fact, one new fertilizer that is mentioned has reached only the pilot-plant stage in Britain, and its effectiveness on crops is still being tested. It is important to remember, however, that the three traditional fertilizers—ammonium sulphate, superphosphate, and potassium chloride—still form the greater part of the fertilizers used, and, while the importance of later developments must not be underestimated, it is fair to say that very great gains indeed have come from investigations on the methods of using the commoner types. With this subject the author deals very fully, and such aspects as the special nutrient requirements of particular crops, and the amounts of fertilizers to use and their residual values, receive excellent treatment.

Dr Smith is to be congratulated on a very useful book. Although it was written primarily for growers and students in agriculture, it will be valued by the specialist also. R. J. WARREN

METALLIC OXIDATION

Oxidation of Metals and Alloys, *by O. Kubaschewski and B. E. Hopkins. Pp. 239. Butterworth's Scientific Publications Limited, London.* 1953. 35*s. net.*

This is a most impressive book, dealing with a subject of great technical importance, about which much is known, but in which there is, as yet, no unifying body of theoretical knowledge. The authors describe their book as written neither from the point of view of the theorist, whose aim is merely to find an atomic mechanism for the processes involved, nor yet that of the production scientist, whose aim is to produce a material to stand up to service conditions; their point of view is intermediate, and they hope that their book will be of assistance to both. It certainly will. The authors have reviewed the widely dispersed literature comprehensively and critically. They have also done justice to such theories as exist. Wagner's work on the theory of oxidation at high temperatures, where the thickness increases according to the parabolic law, seems well established. Some indication of what can happen at lower temperatures is given by the theories of Cabrera and Mott. But about the structure of the oxide and its adhesion to the metal, about recrystallization, and the effects of pores, cracks, and blisters, we have much knowledge but little understanding. The authors consider that, in this branch of science, we appear to be at the threshold of a rapid development of new ideas and theories. I think that they are right, and that this book will greatly help this progress.

N. F. MOTT

INSECTICIDE CHEMISTRY

Insect Control by Chemicals, *by A. W. A. Brown. Pp. 817. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 100*s. net.*

Signalled by the advent of DDT, there has been a spectacular development of synthetic organic insecticides

during the last decade. Those concerned with the problems of insect control now have a bewildering range of insecticides from which to choose. Many factors have to be considered. There may be hazards due to the toxicity of the insecticide to mammals or plants. There may be the possibility of undesirable residues being left on treated foodstuffs. The insect pest may have acquired a serious level of resistance to some insecticides and, in agriculture particularly, there will be economic considerations. These problems and their study have grown with the numbers of available insecticides, together with the need for some co-ordination of the accumulating data. Professor Brown is to be congratulated on his successful attempt to meet this need. His book is probably the most exhaustive survey hitherto made of insecticides and fumigants, their chemistry, pharmacology, and application. In a book covering such a wide range of subjects, from the design of spray nozzles to the neurophysiology of the *Arthropoda*, there are inevitably some mistakes and grounds for criticism. For example, synergism is quite incorrectly defined on p. 299. Carbon disulphide is described as 'highly water-soluble' and classed with hydrogen cyanide in this respect (p. 81). Chapters I and II on chemical properties and relative toxicity to insects might profitably be considerably condensed and arranged in tabular form. Though the relevant literature is on the whole excellently covered, there are some curious gaps. For example, nowhere is the work of Page or of Lubatti mentioned, yet few have contributed so much to the chemistry of fumigation. These blemishes do not, however, impair the great value of the book. Not only is it a mine of information for the entomologist or chemist concerned with insect control, but the appropriate sections will be read with profit by students of the comparative biochemistry and physiology of drug action. The book appears to be expensive, but is not so in relation to the prodigious effort it represents.

F. P. W. WINTERINGHAM

MODERN VACUUM TECHNIQUE

Vacuum Technique, *by Arnold L. Reimann. Pp. xii + 449. Chapman and Hall Limited, London.* 1952. 50*s. net.*

In concluding a section on factors involved in glass-working the author says: 'If glass-work . . . looks good it usually also *is* good.' The reviewer is tempted to make a similar statement about this book. It looks very promising, with its wealth of unusually clear diagrams and well produced photographs, the rich bibliographies at the end of each chapter, and the index of 17 pages in small print—and a closer study of the contents shows that it is very good. On every page it reveals the wide practical experience of the author, whether he describes the great variety of pumps available today and their specific advantages, the best taps and joints, leak-hunting, or precautions in long pumping-runs. His explanations are very clear and, whenever possible, based on theoretical considerations. Three chapters deal with glass and its manipulation, copper-glass seals, and miscellaneous glass-to-metal seals. A final chapter surveys the very different manometers which can be applied in high-vacuum work.

This guide to modern vacuum technique will be found useful not only by those who have to construct complicated vacuum systems and want to attain the greatest efficiency; it is so full of practical hints that workers with more moderate aims will also learn much that will be of immediate use to them, and the first chapter can be recommended to beginners as a very useful introduction to the theory of a technique which is so important in modern science and technology.

F. A. PANETH

CAROTENOID BIOCHEMISTRY

The Comparative Biochemistry of the Carotenoids, *by T. W. Goodwin. Pp.* 356. *Chapman and Hall Limited, London.* 1952. 50*s. net.*

While the pure chemistry of carotenoids has been treated exhaustively in several recent accounts, a modern presentation of the biochemistry of these important natural products has been lacking. This gap is now filled by the excellent book of T. W. Goodwin.

An introduction concerning the definition and nomenclature of carotenoids is followed by part I: carotenoids in plants (carotenoids in land plants, formation and function of carotenoids in phanerogams, carotenoids in other plants). Part II includes animal carotenoids (marine invertebrates; marine vertebrates; fresh-water animals; insects, arachnids, reptiles; mammalian carotenoids; avian carotenoids; conversion of carotenoids into vitamin A). Appendix I contains a very thorough survey of the carotene content of plants, and Appendix II another on the carotene values of a great number of plants, chiefly based on the investigations of R. S. Harris.

Dr Goodwin's work gives an excellent and complete review of the occurrence of carotenoids in the vegetable and animal kingdom, and their relations to biological problems as far as they are known today. It points to gaps which are still waiting to be filled, and takes up a critical position towards many problems. For anyone who is interested in carotenoids and their biochemistry it will be an authentic and necessary aid. A detailed name index, a specific-name index, and a subject index facilitate the orientation and the study of the literature.

One may naturally have a different opinion on certain details. For example, the reviewer believes that the author's opinion that the position of one hydroxyl group in xanthophyll (lutein) is still uncertain cannot be maintained, because its position has been well settled by numerous experimental results.

We owe our thanks to the author for his valuable work, for which a widespread distribution is to be desired.

P. KARRER

THE NEW COSMOLOGIES

The Creation of the Universe, *by George Gamow. Pp. xii + 148, with 40 figures and 11 plates. The Viking Press, New York; Macmillan and Company Limited, London.* 1952. 21*s. net.*

This attractive book will appeal to all who wish to understand recent theories of the origin and evolution of the universe. It is a popular work in the best sense, designed to profit the layman as well as the scientist who works in other fields. Professor Gamow first summarizes such evidence as there is for the ages of the Earth, the stars, and the Milky Way star-system. This evidence all suggests that the universe as we know it today is the outcome of some evolutionary development which began about three thousand million years ago. At this time the universe was compressed into the primeval atom of Lemaître: the 'great expansion' then began, and we can still witness the aftermath of the explosion in the recession of the spiral nebulae. The chemical elements were all built up during this brief period of nuclear gestation, when the universe resembled nothing so much as a giant atom bomb. The alternative ideas, due to Bondi,

Gold, and Hoyle, of a steady-state universe, in which matter is being continuously created as fast as it is thinned out by expansion, are rather summarily dismissed. Likewise, Hoyle's theory of atom-building in supernovae is rejected, since it does not harmonize with the author's evolutionary scheme.

We make one criticism. The reader must keep his critical faculty on the alert. Here and there the author writes so persuasively that he allows his speculations to derive quite unwarranted support from uncertain observations. Thus, for example, we read: 'Hubble found that the galaxies populating the space of the universe are in a state of rapid dispersion ("expanding universe").' Or, again: 'The relationship between recession velocity and distance is given by Hubble's law. . . .' Now, Hubble has been most careful to point out ('The Realm of the Nebulae') that all we can observe are red-shifts in the nebular spectral lines and that these appear to increase with distance. The red-shifts may be interpreted as indicating velocities of recession, and they have been seized upon in this sense by many cosmologists in order to save the theory of the expanding universe. Equally well, they may arise from the action of some unrecognized principle leading to loss of photon energy in intergalactic space. Our ignorance in this field is so complete that it is wise to suspend judgment until further observations can decide the issue.

M. A. ELLISON

FATS AND LIPIDS

Progress in the Chemistry of Fats and Other Lipids, *edited by R. T. Holman, W. O. Lundberg, and T. Malkin. Vol. I. Pp. vii + 186. Pergamon Press Limited, London.* 1952. 42*s. net.*

Little more than a century ago Watt's 'Dictionary of Chemistry' covered the whole of chemistry, pure and applied, in two or three volumes. Fifty years ago, the single field of the chemistry and technology of oils, fats, and waxes was dealt with in a few volumes by Lewkowitsch, Ubbelohde, or Hefter. Now it has been found desirable to issue a much larger number of monographs on fats and related materials, in two series, one dealing with the chemistry and the other with the technology of this important group of organic compounds.

This book is the first to be published in the purely chemical series. It contains five sections, devoted respectively to polymorphism of fatty acids (T. Malkin), the sterols (W. Bergmann), the phosphatides (P. Desnuelle), chromatography of fatty acids (R. T. Holman), and various chemical derivatives of fatty acids (H. J. Harwood). Each section contains a complete account down to the most recent work on its subject, and the quality of the articles is uniformly of a very high order, as indeed would be expected from the authorities to whom the respective topics have been entrusted. The treatment throughout is extremely clear and up-to-date, and the volume is excellently printed, with full literature references and adequate indexes.

The choice of subjects is rather haphazard (doubtless for accidental reasons suggested in the editorial preface). It may be hoped, however, especially in view of the cost of the volumes in this series, that in further monographs some attempt will be made to introduce a more systematic selection of related topics in any one volume. Readers, who will include students and investigators requiring a full account of specific branches of lipid chemistry, will find greater convenience if each volume is made to include five or six aspects of the subject which have some general connection with each other. Apart from this, the book deserves full commendation. The appearance of further companion volumes will be awaited with interest by all concerned with this province of chemistry.

T. P. HILDITCH

STRUCTURE REPORTS

Structure Reports for 1949, *Vol. XII. General Editor: A. J. C. Wilson; Section Editors: C. S. Barrett, J. M. Bijvoet, and J. M. Robertson. Pp. viii + 478, with numerous figures. Oosthoek, Utrecht.* 1952. 90*s. net.*

'Structure Reports,' which are not abstracts in the ordinary sense, extract only the material of structural interest in the papers reported, and do this so completely that no further structural information is to be gained by consulting the paper itself. Such is the standard. Three main sections—metals, inorganic compounds, and organic compounds—cover a wide range of papers, including those in Russian and Japanese and some information from declassified U.S. atomic energy commission publications. In places also, abstractors mention private communications. Structural information may include a complete phase diagram, and is not restricted to X-ray crystallographic material. Under organic compounds, a number of electron-diffraction investigations are noticed. Tables, diagrams, and indexes are of high quality.

That the reports are critical is evident from a number of recalculations and additional calculations from authors' figures, and from editorial remarks when an author's listed absent spectra are in doubtful agreement with his stated space-group (as for the mineral wittichenite). It would be surprising if the abstractor's eye were always so keen. The section on acenaphthene could, with advantage, have mentioned that the space-group is chosen from three alternatives by use of the theory of close packing, and that the structure determination is based on an unnecessary assumption of special positions for the molecules. Such details are the more valuable, the less familiar the language of the original paper. This section notes the author's inconsistent values, 2·375 A in a figure and 2·355 A in the summary, for the width of the benzene ring, but adds a new complication by giving the CH_3—CH_3 bond distance as $1{\cdot}64 \pm 4$ A [$\pm$ 0·4].

A work by many collaborators, some of whom do not have English as their first language, might be expected to show irregularity of style and usage, but there is no significant evidence of it. The word 'ordinally' planted in the first paragraph of the introduction is clearly a trap for the reviewer, being merely misprinted from the corresponding sentence in the introduction to volume XI, but perhaps 'recommanded' on p. 129 is a genuine continental product.

In one place there is a familiar ring about 'data' used for 'experimental results,' and in another there is an English echo of a foreign tongue where we read of 'a stage prior to the formation of a precipitate strict sense.' *Proprement dit*, this is what Dr Guinier wrote; but *proprement dit*?

Such minor blemishes may be accorded the status of honorary embellishments in a work which as a whole shows the greatest care. The reports achieve their aim, and will be invaluable to all, whether crystallographers or not, who seek information on crystal and molecular structures. Heartily *recommanded.*

H. M. POWELL

THE RIDDLE OF DEVELOPMENT

Morphogenesis: An Essay on Development, *by J. T. Bonner. Pp.* 296, *with line and half-tone illustrations. Princeton*

University Press, Princeton, New Jersey; Oxford University Press, London. 1952. 32*s.* 6*d. net.*

This book is essentially a series of discussions of the inception of form and structure in plants and animals. The scope and contents of the book may be briefly indicated by the fact that particular chapters are concerned with a consideration of size and pattern, the physics and chemistry of development, patterns of growth, morphogenetic movement and differentiation, polarity and symmetry, and an analysis of development. Obviously, in this comparatively short book, only a limited treatment of what has become a very important theme in contemporary biology has been possible. But, because he has thought deeply, the author has been able to express in this essay much that is cogent. By the use of carefully selected examples, he has shown what is implied, and required, in any attempt to provide satisfying causal explanations of the processes involved in morphogenesis. In the development of different species, different factors may be involved in comparable morphogenetic developments, as, for example, in the determination of polarity; but there are some common phenomena which appear to be universal, and, for at least some of them, explanations can be suggested. To Dr Bonner, the inception of form is a result of the constructive processes of growth, morphogenetic movement, and differentiation, and the limiting of these processes by various factors. An important feature of this book is the author's discussion of what he describes as a microtheory of morphogenesis, i.e. a theory in which organismal development, with its many repetitive features, could be referred to relatively small units. At this stage, the facts scarcely admit of conjectures concerning the details of a microstructure theory; and indeed it may be doubted if this kind of theory would deal adequately with the complex phenomena of morphogenesis. Nevertheless, the idea is thought-provoking, and its further pursuit can hardly fail to be attended with interesting results. This thoughtful book can be recommended to the general reader as well as to those who are specially engaged in this challenging field.

C. W. WARDLAW

MARINE ZOOGEOGRAPHY

Zoogeography of the Sea, *by Sven Ekman. Pp. xiv* + 417, *with* 121 *figures. Sidgwick and Jackson, London.* 1953. 42*s. net.*

This is one of the most important books dealing with marine animals which has ever appeared. It was first published in German in 1935, by the *Akademische Verlagsgesellschaft* of Leipzig, and has not hitherto been either as widely read or as fully appreciated in English-speaking countries as it deserves. The very welcome appearance of this English edition should remedy these shortcomings. The present version has not merely been translated, but has been revised very thoroughly so as to incorporate a great deal of work published since 1935. It now represents the most comprehensive existing account of the distribution of marine faunas in the various seas of the world, and will make available to zoologists a wealth of material not hitherto accessible in English. It also represents a distinctive point of view, and provides a most interesting education in animal geography. The ground covered includes a survey of the bottom-fauna of the deep sea; of the pelagic faunas of the upper layers and of the deeper waters; and a discussion of questions of bipolarity and 'longitudinal distribution'; but more than half the book (230 pages) deals with the faunas of the shallower seas of the world. These faunas are discussed regionally in a number of chapters, and not only is their present distribution considered, but their past history is taken into account in enough detail to make the existing distribution intelligible. The book is well illustrated and translated. Probably some of the conclusions set forth for particular countries will prove incorrect or inadequate as knowledge develops, but this is a matter of detail which in no way detracts from the general value of the book.

T. A. STEPHENSON

SURFACE CHEMISTRY

The Physical Chemistry of Surface Films, *by William D. Harkins. Pp. xvi* + 413, *with an introduction by T. Fraser Young. Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1952. 80*s. net.*

This book is an account of the author's extensive researches in surface chemistry, including much beyond what is ordinarily included under the title of surface films. Harkins' first publication on surfaces was in 1915, his last in 1950, and there are some two hundred of them—a very fine record of industry. The first six years were devoted to a study of accurate methods of measuring surface tension, and the measurement of surface tensions and interfacial tensions against water, or mercury, of a large number of organic liquids. Harkins established the conditions under which the drop-volume method gives accurate results, and his tables for calculating the results are still standard. His calculations of the work of adhesion confirmed the view, earlier put forward by W. B. Hardy, that molecules are oriented at the interfaces; he is not fair, however, when he says that Hardy gave no evidence in favour of this orientation. In fact, Hardy's evidence was of exactly the same kind as Harkins', only Harkins, publishing a few years later, gave much more of it. Later, Harkins turned his attention to many problems, including standardization of the 'ring' method for measuring surface tensions, study of the heat of adsorption of liquids on solids, of contact angles, and of methods for determining the surface area of powdered solids. He also did a good deal of accurate work on insoluble monolayers, the most original part of this being on the effect of traces of ions in the water, and on the viscosity of the surface films. In the last few years he studied the internal constitution of soap solutions, and emulsion polymerization, and found a very simple colorimetric method for determining the critical concentration for formation of ionic micelles.

All the experimental work is careful, and though part of it may at first seem only a minor continuation of some research established by others, Harkins practically always introduced improvement in technique, and often his work attained greater precision than was achieved by anyone else.

Brief reference is made to topics on which the author had not himself worked, and the book ends with a chapter by Verwey, summarizing the work of the Dutch school on the effect of ions on the electrical double layer and the stability of lyophobic sols. Harkins worked in so many different branches of surface chemistry that the book is quite a good general textbook of the subject. Rightly, he emphasizes his own points of view, but the distinction of the book is somewhat marred by his habit of depreciating the importance of previous work, and over-emphasizing the importance of his own, even when he has only varied the technique in

some detail or worked on a more extensive scale than others. As a record of the work of one of the keenest researchers of his generation, who has made many contributions of lasting importance to this branch of science, it should be carefully studied by all mature students of surface chemistry. The price is regrettably high, and may put the book out of reach of many individuals and some libraries, where it could be of great value.

N. K. ADAM

HYDROGEN ION CONCENTRATION

Hydrogen Ion Concentration, *by John E. Ricci. Pp.* 460, *with line diagrams. Princeton University Press, Princeton, New Jersey; Oxford University Press, London.* 1952. 63*s. net.*

The author of this book presents a very exhaustive and detailed treatment of the problem of hydrogen ions in solution. Most of us tend to regard the processes of dissociation and ionization as identical when we discuss the question of the state of electrolytes in solution. The author rightly points out that the presence of hydrogen and chlorine ions in an aqueous solution of hydrogen chloride does not necessarily imply the dissociation of the hydrogen halide, as the formation of a hydrated chlorine ion might be formed from water by a reaction $HCl + OH' \rightarrow HOHCl'$, leaving the aqueous hydrogen ion as the oppositely charged partner. Dissociation, on the other hand, is clearly present in aqueous solutions of salts. He also introduces the concept of a charge coefficient, being the net number of foreign solute ionic charges of one sign produced per mole of dissolved solute. While it takes a little effort to accustom oneself to the method of treatment adopted by Ricci, it is an exact method and permits one to develop the fundamental relations based on the mass law in a precise manner.

Excellent accounts are given concerning the sharpness of titration, buffer capacity, and the titration of mixtures.

The last five sections of the volume are devoted to problems in which the solubility product of at least one ion-pair imposes a limitation on the system. It is in this field that the author's method of attack reveals itself to be most powerful, since the boundaries of the phase system can be accurately developed.

This book should find a place on the shelves of all those whose field of work lies in the domain of electrolytic equilibria. It is well printed and free from errors, and its price is not unreasonable in the present spiral of costs.

ERIC K. RIDEAL

THE OPOSSUM

Possums, *by Carl G. Hartman. Pp.* 174, *with half-tone and line illustrations. University of Texas Press, Austin, Texas.* 1952. $6 net.

In the opossum, as in all marsupial mammals, the young are born while still in a very rudimentary stage of development—they have been described as 'veritable abortions.' Not more than twenty-four hours after the naked ovum or yolk comes from the ovary, it becomes covered with albumen and a shell membrane. At the end of seven days the egg has become a hollow vesicle lined with three cell-layers, but only a tiny rudiment of the embryo is present, although half of the intra-uterine life has already passed. In six more days the embryos have to be ready for birth and their precarious trip to the pouch; the development from a delicate vesicle smaller than a pin-head to a new-born opossum requires only this short time.

The details of these processes and the pictures illustrating them are the highlights of Dr Hartman's fascinating book, for he was the first man to observe them and record them in their entirety. But this is no technical study interesting only to the specialist: it is the complete life-history of one of the world's strangest animals, written simply but accurately for the general reader by the man who knows more about the subject than anyone else.

Dr Hartman deals with the opossum in history and legend, and in real life; he has chapters on 'playing 'possum,' on the dangerous journey to the mother's pouch of the new-born young (a litter of twenty comfortably lies on a teaspoon), 'possum hunting, recipes for cooking 'possum and 'taters,' the 'possum in negro folk-lore, and much else besides.

The book is beautifully illustrated with pictures, and illuminated by the author's genial personality. If ever a book deserved to become a classic of natural history and a best seller, Carl Hartman's 'Possums' does.

L. HARRISON MATTHEWS

THE PROCESS OF EVOLUTION

Evolution in Action, *by J. S. Huxley. Pp.* 160, *with* 9 *half-tone plates. Chatto and Windus, London.* 1953. 9*s.* 6*d. net.*

Huxley's most recent book is based on a series of lectures given at Indiana University in 1951 under the auspices of the Patten Foundation, and repeated in a modified form as broadcasts disseminated by the B.B.C. He has attempted a very difficult task—nothing less than to present 'some sort of map of the evolutionary process as a whole.' No one could do this quite faultlessly in a mere 160 pages, but Huxley's achievement is remarkably impressive. His success is based not only on a very wide knowledge of the technical facts, but on a clear formulation of the kind of picture which he wished to build up. He has not tried to develop a fully convincing and logical theory of the detailed processes of evolution, but has aimed at conveying a general picture of its nature, from which one can get a bird's-eye view not only of the mechanisms of both long- and short-term changes, but of their results. It is a particularly important feature of the book that a considerable proportion of it is devoted to a discussion of human evolution and its relation to that of non-human organisms. Huxley sees the development of human life since its earliest beginnings as a continuation of biological evolution, but he lays stress on the profound difference in the mechanism on which it depends; whereas in the sub-human realm the only effective mode of inheritance is by means of genes, in human affairs the transmission of ideas and inventions by cultural means is much more important. Huxley is also bold enough to tackle the question of whether there is any sense in which one can usefully speak of 'progress' during the course of evolution, an idea which necessarily raises the problem of values. He makes the useful suggestion that we must distinguish between progress and mere improvement which fits an animal better to meet some particular restricted demand. His discussion of the whole thorny question is, perhaps, not philosophically watertight, and indeed it would have been out of place to have attempted such a treatment in this book, but it is eminently good common sense, and is likely to prove very enlightening to the general reader to whom it is addressed.

C. H. WADDINGTON

Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review.)

AGRICULTURE

British Farming 1939–49, *by E. H. Whetham. Pp.* 172. *Thomas Nelson and Sons Limited, London.* 1953. 12*s.* 6*d. net.*

Soil Restoration, *by Edward Faulkner. Pp.* 207. *Michael Joseph, London.* 1953. 10*s.* 6*d. net.*

Wood Chemistry (*2nd ed.*), *Vols. I and II, edited by Louis E. Wise and Edwin C. Jahn. Pp.* 1–688 *and* 691–1343 *respectively. Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1952. 120*s. each volume.*

ASTRONOMY

Astronomy for Everyman, *edited by Martin Davidson. Pp.* 494. *J. M. Dent and Sons Limited, London.* 1953. 18*s. net.*

The Comets and their Origin, *by R. A. Lyttleton. Pp.* 173. *Cambridge University Press, London.* 1953. 25*s. net.*

BIOLOGY

La Greffe, *by Raoul-Michel May. Pp.* 299. *Gallimard, Paris.* 1953. *Fcs.* 900.

The Neuron; Cold Spring Harbor Symposia on Quantitative Biology, *Vol. XVII. Pp. xiv* + 324. *The Biological Laboratory, Cold Spring Harbor, New York.* 1952. $8 *net.*

Protein Metabolism, Hormones and Growth. A Symposium. *Pp.* 80. *Rutgers University Press, New Brunswick, New Jersey.* 1953. $1.50 *net.*

CHEMISTRY

Dissociation Energies and Spectra of Diatomic Molecules (*2nd ed.*), *by A. G. Gaydon. Pp.* 261. *Chapman and Hall Limited, London.* 1953. 35*s. net.*

The Dynamical Character of Adsorption, *by J. H. de Boer. Pp.* 239. *Oxford University Press, London.* 1953. 30*s. net.*

Kinetics and Mechanism, *by Arthur A. Frost and Ralph G. Pearson.* Pp. 343. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1953. 48*s. net.*

Organic Syntheses, *Vol.* 32, *edited by R. T. Arnold. Pp.* 119. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1953. 28*s. net.*

Proceedings of the International Congress on Analytical Chemistry. Oxford, 4th–9th Sept., 1952. *Pp.* 493. *Published for the International Congress on Analytical Chemistry and the Society of Public Analysts and Other Analytical Chemists by W. Heffer and Sons Limited, Cambridge.* 1953. 42*s. net.*

Semi-Micro Apparatus and Technique, *by H. Holness. Pp.* 19. *Sir Isaac Pitman and Sons Limited, London.* 1953. 2*s. net.*

Soluble Silicates: Their Properties and Uses, *Vol. II: Technology, by James G. Vail. Pp.* 669. *Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1952. 120*s. net.*

Starch and its Derivatives (*3rd ed.*), *Vol. I, by J. A. Radley. Pp.* 510. *Chapman and Hall Limited, London.* 1953. 65*s. net.*

Substances Naturelles de Synthèse, *Vols. I–V, edited by Léon Velluz. Pp.* 141, 138, 156, 165, *and* 206 *respectively. Masson et Cie., Paris.* 1951–3. *Fcs.* 1750, 1750, 1750, 2200, *and* 2800 *respectively.*

A Textbook of Pure and Applied Chemistry, *by James E. Garside and R. F. Phillips. Pp.* 1044. *Sir Isaac Pitman and Sons Limited, London.* 1953. 25*s. net.*

Volumetric and Phase Behaviour of Oil Field Hydrocarbon Systems, *by M. B. Standing. Pp.* 123. *Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1952. 80*s. net.*

GENERAL

Schmuck- und edelsteinkundliches Taschenbuch, *by Karl F. Chudoba and Eduard J. Gübelin. Pp.* 206, *with two colour plates. Verlag Bonner Universitäts-Buchdruckerei Gebr. Scheur G.m.b.H., Bonn.* 1953. DM 19.60 *net.*

The Scientists Look at Our World, *edited by John M. Fogg, Jr. Pp.* 147. *University of Pennsylvania Press, Philadelphia.* 1952. $3 *net.*

GEOGRAPHY

Between Pacific Tides (*3rd ed.*), *by Edward F. Ricketts and Jack Calvin. Pp.* 502. *Stanford University Press, California; Oxford University Press, London.* 1953. 48*s. net.*

The Ocean River, *by Henry Chapin and F. G. Walton Smith. Pp.* 325. *Victor Gollancz Limited, London.* 1953. 16*s. net.*

HISTORY OF SCIENCE

Buffon, *by L. Bertin, F. Bourdier, E. Dechambre, Y. François, E. Genet-Varcin, G. Heilbrun, R. Heim, J. Pelseneer, and J. Piveteau. Pp.* 244. *Publications Françaises, Paris.* 1953. *Fcs.* 900.

Robert Grosseteste and the Origins of Experimental Science 1100–1700, *by A. C. Crombie. Pp.* 369. *Oxford University Press, London.* 1953. 35*s. net.*

A History of Science—Ancient Science through the Golden Age of Greece, *by George Sarton. Pp.* 646. *Oxford University Press, London.* 1953. 63*s. net.*

A History of the American Chemical Society, *by Charles Albert Browne and Mary Elvira Weeks. Pp.* 526. *The American Chemical Society, Washington, D.C.* 1952. $5 *net.*

MEDICINE

British Pharmacopoeia, 1953. *Published under the direction of the General Medical Council. Pp.* 894. *The Pharmaceutical Press, London.* 1953. 50*s. net.*

Man and Epidemics, *by C. E. A. Winslow. Pp.* 246. *Princeton University Press, New Jersey; Oxford University Press, London.* 1952. 25*s. net.*

The Neurophysiological Basis of Mind, *by J. C. Eccles. Pp.* 314. *Oxford University Press, London.* 1953. 25*s. net.*

Traité Elémentaire de Physiologie Humaine (*3rd ed.*), *by Henri Fredericq. Pp.* 812. *Masson et Cie., Paris; H. Vaillant-Carmanne S.A., Liège.* 1952. *Fcs.* 4000.

PHYSICS

Annual Review of Nuclear Science, *Vol. II,* 1953. *Pp.* 429. *Annual Reviews Inc., Stanford, California.* 1953. $6 *net.*

High-Energy Particles, *by B. Rossi. Pp.* 569. *Prentice-Hall Inc., New York; Constable and Company Limited, London.* 1953. 65*s. net.*

Photometry (*2nd ed.*), *by John W. T. Walsh. Pp.* 544. *Constable and Company Limited, London.* 1953. 63*s. net.*

Progress in Nuclear Physics, *Vol. II, edited by O. R. Frisch. Pp.* 295. *Pergamon Press Limited, London.* 1953. 63*s. net.*

Stress Waves in Solids, *by H. Kolsky. Pp.* 211. *Oxford University Press, London.* 1953. 25*s. net.*

TECHNOLOGY

British Plastics Year Book 1953: A Classified Guide to the Plastics Industry. 23*rd edition. Pp.* 562. *Iliffe and Sons Limited, London.* 1953. 30*s. net.*

The Cathode Ray Oscillograph in Industry (*4th ed.*), *by W. Wilson. Pp.* 273. *Chapman and Hall Limited, London.* 1953. 36*s. net.*

Notes on contributors

SIR HENRY DALE,
O.M., G.B.E., F.R.S.,

Was born in 1875 and was educated at the Leys School and Trinity College, Cambridge, and at St Bartholomew's Hospital. After holding postgraduate scholarships at Cambridge, Frankfurt-am-Main, and London, entered the Wellcome Physiological Research Laboratories in 1904, being director from 1906 to 1914. In the latter year was appointed an original member of the staff of the National Institute for Medical Research, which he directed from 1928 to 1942. His main researches derive ultimately from a study of the pharmacology of ergot begun in 1904, and deal with the chemical transmission of nervous effects and with histamine, anaphylaxis, and allergy. Was elected to Fellowship of the Royal Society in 1914; was Secretary from 1925 to 1935 and President from 1940 to 1945. In 1936 he shared the Nobel Prize for physiology and medicine. Since 1937 has been chairman of the Wellcome Trustees. In 1940 was made member of the Scientific Advisory Committee to the War Cabinet, and was its chairman from 1942 to 1947. He was member of the Advisory Committee on Atomic Energy from 1945 to 1947.

W. G. PALMER,
M.A., Sc.D.

Fellow of St John's College, Cambridge. University Lecturer in the Department of Inorganic and Organic Chemistry, Cambridge. Author of 'Experimental Physical Chemistry,' 'Valency—Classical and Modern,' and 'Experimental Inorganic Chemistry' (forthcoming).

D. McKIE,
Ph.D., D.Sc.,

Was born in Monmouthshire in 1896. He entered University College, London, in 1920 and graduated in chemistry. Now reader in the history of science in the University of London. Has written extensively on the history of chemistry, including an authoritative book on Lavoisier's life and work.

C. H. WADDINGTON,
M.A., Sc.D., F.R.S.,

Was born in 1905 and was educated at Clifton College and Sidney Sussex College, Cambridge. After graduation he undertook biological research, studying the evolution of fossils, the genetics of plants, and the development of animals. He has travelled extensively and collaborated with scientists in many foreign countries. Besides contributing about fifty papers to scientific journals he is the author of several books: 'How Animals Develop,' 'Introduction to Modern Genetics,' and 'Organisms and Genes.' During the war he was scientific adviser to the Commander-in-Chief of Coastal Command, Royal Air Force. In 1947 he was appointed to the professorship of animal genetics in the University of Edinburgh, and in this capacity he is responsible for directing the work of a considerable number of scientists financed by the Agricultural Research Council.

K. MATHER,
D.Sc., F.R.S.,

Was born in 1911, and was educated at Nantwich and Acton Grammar School and the University of Manchester. He has carried out research upon plant breeding at Svalöf (Sweden), and was Rockefeller Fellow at the California Institute of Technology and at Harvard University in 1937–8. In 1938 he was appointed head of the genetics department of the John Innes Horticultural Institution, leaving this position in 1948 to become the first professor of genetics in the University of Birmingham. In 1949 he was appointed to membership of the Agricultural Research Council. Mainly concerned with the genetics of those quantitative or polygenic characters basic to evolutionary theory and to the practice of plant and animal improvement, he has also written books on statistics, and believes that all students of biology should be taught the principles of statistical analysis as an essential part of their training in experimental science.

W. B. ALEXANDER,
M.A.

Born at Croydon in 1885. Educated at Bootham School, York, Tonbridge School, and King's College, Cambridge. From 1912 to 1926 he held various biological posts in Australia, first in Western Australia and later under the Commonwealth Government.

In 1930 he began research in economic ornithology, and in 1939 was appointed first director of the Edward Grey Institute of Field Ornithology, University of Oxford. Since retirement in 1945 he has continued to act as librarian of the Institute.

Author of 'Birds of the Ocean,' 1928; Fellow of the Royal Australasian Ornithologists' Union; Corresponding Fellow of the American Ornithologists' Union; member of council, and chairman of the Bird Observatories Committee, of the British Trust for Ornithology.

B. W. MOTT,
M.A.

Born in 1919. Educated at Oundle Laxton Grammar School, and Christ's College, Cambridge. After two years with High Duty Alloys, he joined the Royal Aircraft Establishment, Farnborough, where he was leader of a team engaged in research and development work on light alloys. In 1945, he was leader of a number of Combined Intelligence objectives sub-committee teams investigating technical developments in Germany during the war. Since 1946, he has been at the Atomic Energy Research Establishment, Harwell, in charge of a group working on the alloying behaviour of the heavy elements and investigating new metallographic techniques. He has published several papers dealing with aluminium alloys and developments in metallography.

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